The selective chlorination of phenols using novel thiapolymers as catalysts.

Williams, Des

THE SELECTIVE CHLORINATION OF PHENOLS USING NOVEL THIAPOLYMERS AS CATALYSTS

By

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Summary

Extensive work on enhancing the regioselectivity of electrophilic aromatic substitution reactions has been conducted at the Centre for Clean Chemistry, University of Wales Swansea. As a continuation of that work, this project involves the development of regioselective methods for the chlorination of phenols.

Previous results conducted at the Centre for Clean Chemistry have shown that polythiaalkanes behave as highly selective catalysts for the chlorination of phenols with sulfuryl chloride.

The work reported in this thesis involves the syntheses of numerous novel thiapolymers, containing branched chains, cyclic aliphatic rings and aromatic rings. These novel polymeric materials were tested as catalysts for the chlorination of phenol, *o*-cresol, *m*-cresol and *m*-xylenol.

The first chapter gives an extensive introduction to aspects of the selective chlorination of phenols and a brief introduction to green chemistry and polymer synthesis.

The second chapter reports the development of synthetic routes to some novel branched thiaalkanes from secondary dibromides. The synthesised novel branched thiapolymers were shown to be, above all, excellent selective catalysts for the chlorination of *m*-xylenol.

The third chapter reports the synthesis of branched polymers and cyclic tetrahydrothiopyrans from methyl substituted 1,5-dibromopentanes. The branched polymeric materials synthesised were shown to behave as mediocre catalysts for the chlorination of phenols. However, the cyclic sulfides synthesised were shown to be excellent selective catalyst for the chlorination of *o*-cresol and also good selective catalysts for the chlorination of phenol and *m*-cresol.

The fourth chapter reports the syntheses of thiapolymers containing cyclic aliphatic and aromatic rings. The novel cyclic aliphatic containing thiapolymers proved to be very effective selective catalysts for the chlorination of phenols with excellent results for the chlorination of *o*-cresol, and good results for the chlorination of *m*-cresol and *m*-xylenol obtained. Some of the novel aromatic containing polymers were also shown to be selective catalysts for the chlorination of *o*-cresol.

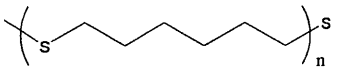
Chapter Guide

For full contents please turn to the back.

Abbreviation List

2,4-D	2,4-Dichlorophenoxyacetic acid
BTMS	Bromotrimethyl silane
CFC	Chlorofluorocarbon
CI	Chemical Ionisation
CPD	Composite-Pulse Decoupling
CTMS	Chlorotrimethyl silane
DCM	Dichloromethane
DCMS	Chlorodimethylsulfonium chloride
DCMX	Dichloro-*meta*-xylenol (2,4-dichloro-3,5-dimethylphenol)
DCP	Dichlrophenol (2,4-dichlorophenol)
DCPM	Dichlorophenoxymethane
DDT	Dichlorodiphenyldichloroethane
DEPT	Distortionless Enhancement by Polarization Transfer
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
EI	Electron Impact (ionisation)
ES	Electrospray (ionisation)
FTIR	Fourier Transform Infrared spectroscopy
GC	Gas Chromatgoraphy
GPC	Gel Permeation Chromatography
HPLC	High Pressure Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
LAH	Lithium aluminium hydride
MALDI	Matrix Assisted Laser Desorption (ionization)
MC	*meta*-Cresol (3-methylphenol)
MCPA	4-Chloro-2-methylphenoxyacetic acid
MX	*meta*-Xylenol (3,5-dimethylphenol)
OC	*ortho*-Cresol (2-methylphenol)
OCMC	*ortho*-Chloro-*meta*-cresol (2-chloro-3-methylphenol and 2-chloro-5-methylphenol)
OCMX	*ortho*-Chloro-*meta*-xylenol (2-Chloro-3,5-dimethylphenol)
OCOC	*ortho*-Chloro-*ortho*-cresol (2-chloro-6-methylphenol)
OCP	*ortho*-Chlorophenol (2-chlorophenol)
P	Phenol
PCC	Pyridinium chlorochromate
PCMC	*para*-Chloro-*meta*-cresol (4-chloro-3-methylphenol)
PCMX	*para*-Chloro-*meta*-xylenol (4-chloro-3,5-dimethylphenol)
PCOC	para-Chloro-*ortho*-cresol (4-chloro-2-methylphenol)
PCP	*para*-Chlorophenol (4-chlorophenol)
PPS	Poly(phenelyne sulfide)
PVC	Polyvinyl chloride
SEC	Size Exclusion Chromatography
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography

Reference guide to polymer structures and nomenclature used in this thesis.



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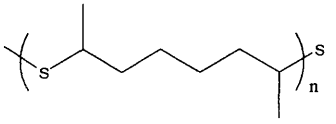

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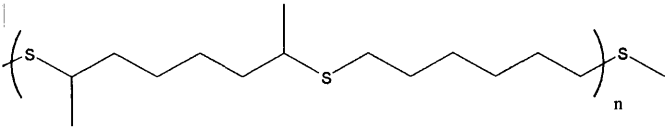

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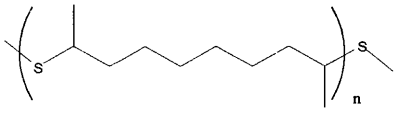

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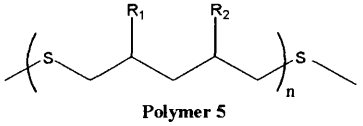

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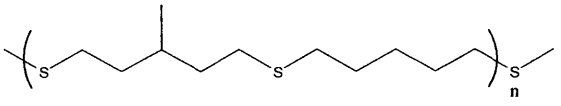

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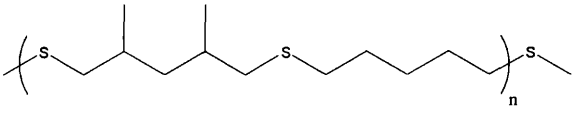

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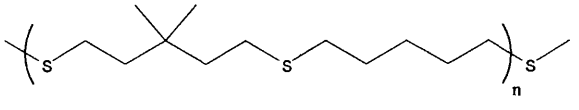

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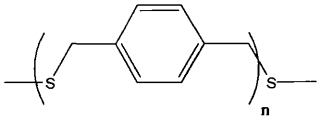

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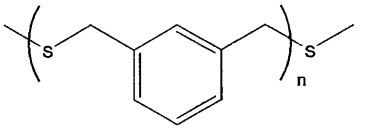

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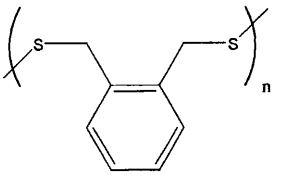

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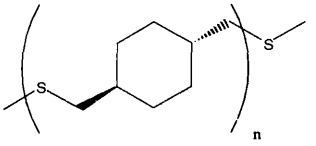

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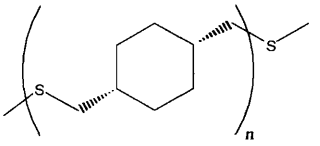

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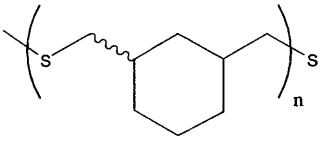

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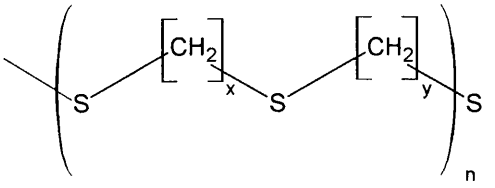
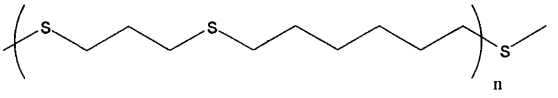


Polymer x-y

Linear polythiaalkanes are named in accordance to the size of the aliphatic spacer subunits. For example when x = 3 and y = 6 then the polymer is termed Polymer 3-6. IUPAC recommended nomenclature for polymeric compounds is used in the experimental section. For more details see Section 2.2.



Polymer 3-6

Chapter 1: Introduction to the selective chlorination of phenols using novel thiapolymers.

1.1 Opening remarks

Chlorinated organic compounds are versatile compounds that have numerous applications in the chemical industry. In recent times the environmental effects of such compounds have been closely investigated. CFC's and DDT have been important compounds that have led to the general understanding that chlorinated organic compounds have the potential to persist in the environment and cause damage to life or the atmosphere.

Where feasible, alternative compounds have been used to reduce the volume of chlorine containing compounds required in industrial applications, and therefore reduce the potential hazard they can impact on the environment.

However, the negative image of chlorine containing compounds has recently been played down, by the controversial claims that chlorine is the only green element.[1]

Regardless of strategies to phase out chlorine containing chemicals, many such chemicals still have wide scale industrial use, including chemicals such as chlorinated phenols.

The production and use of chlorinated phenols is a well-established and desirable industrial objective. The resultant products are used on a wide scale with diverse applications, for production or use as pesticides, herbicides, dyestuff, disinfectants and antiseptics.

Traditional production methods[2] involve the use of solvents, molecular chlorine, and stoichiometric amounts of catalysts or co-reagents. Product mixtures contain various unwanted isomers that are difficult to separate, which ultimately lead to the loss of material and increased costs of production.

In more recent years emphasis has been placed on the development of 'greener' alternatives for production. Common strategies employed involve the use of more selective chlorinating agents, solvent free conditions, and catalytic amounts of selective catalysts, co-reagents or solid supports.

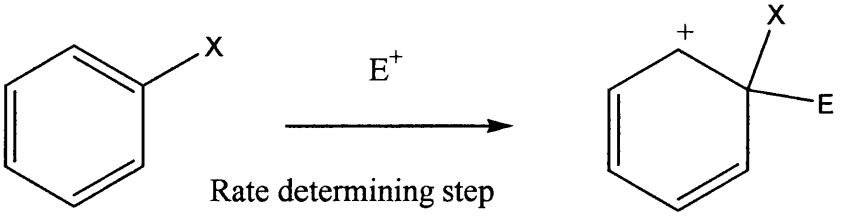
At the present time there is no commercially attractive industrial process for the production of chlorinated phenols that significantly appeals to the principles of green chemistry, and therefore, it is in our interest to continue the pursuit to create such a process.

This introduction gives an overview of the important concepts and chemistry involved in the selective chlorination of phenols, and includes a review of previous strategies employed, with particular interest on the use of divalent sulfur compounds in the presence of sulfuryl chloride. A brief introduction to aspects of green chemistry and polymer synthesis is also included in this chapter.

1.2 Electrophilic aromatic substitution: Mechanism, reactivity and selectivity.

Benzene is a notoriously stable compound due to aromaticity, and consequently its double bonds do not undergo addition like isolated double bonds without conjugation, but benzene does undergo substitution, electrophilic aromatic substitution. Owing to the importance of aromatic compounds in synthetic chemistry, the mechanism of this substitution has been widely studied.[3] The electrophilic aromatic substitution process is sometimes described as S_E2 as it is bimolecular, but this terminology is usually more associated with aliphatic substrates. The IUPAC term for the mechanism is $A_E + D_E$.

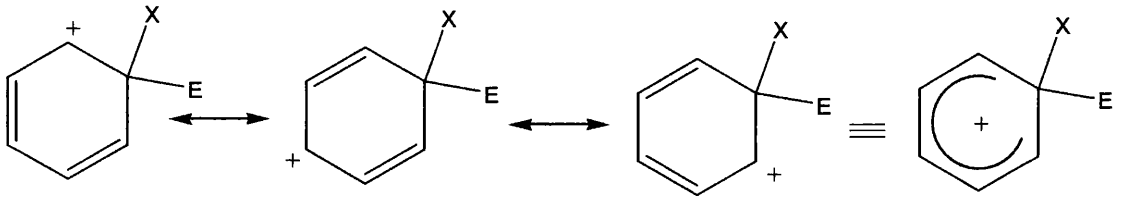
The electrophile attacks in the first step (slower step), removing a pair of π electrons from the ring, creating a carbocation intermediate, sometimes called a Wheland intermediate, or an arenium ion, the latter of which terms will be used in this thesis. In the case of benzene the intermediate is a cyclohexadienyl cation (**1**, Scheme 1.1).



1

Scheme 1.1: Formation of an arenium ion (**1**).

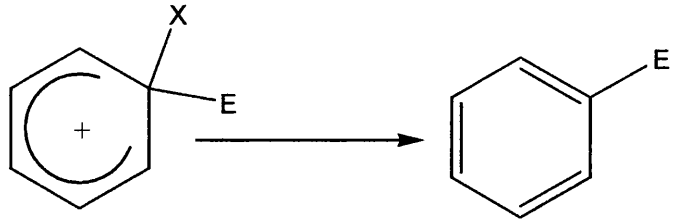
The formation of the arenium ion (**1**) and therefore the loss of aromaticity from the ring system is unfavourable thermodynamically, but the relatively unstable cation formed stabilizes itself by resonance (Scheme 1.2).



1

Scheme 1.2: Resonance stabilised arenium intermediate (**1**).

Even with this resonance stabilisation, the arenium ion is still unstable relative to an aromatic system, therefore either X or E must act as a leaving group to regenerate the aromatic ring. The best leaving groups for this substitution are groups that can leave without the pair of electrons needed to fill their outer shell, such as a proton. Therefore the most common situation is electrophilic attack followed by proton abstraction. This occurs generally much more quickly than the first step (Scheme 1.3), making the first step (Scheme 1.1) the rate determining step, resulting in second order kinetics.



1 **2**

Scheme 1.3: The fast step in the electrophilic aromatic substitution mechanism driven by the regeneration of the aromatic ring (**2**).

Proof for the arenium ion has been provided by various isotope effect investigations [4] and by isolation and spectral studies. For example Olah trapped **3** as a solid (Figure 1.1).[5]

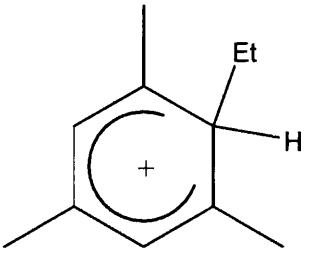


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Figure 1.1: Arenium species (**3**) isolated by Olah.[5]

Compound **3** was trapped using EtF as the electrophile and BF_3 as the catalyst at a very low temperature. When the compound was allowed to warm up the expected substitution product formed.

Olah has also used ^{13}CNMR to study the benzenonium ion **4** at -137°C (Figure 1.2).[6]

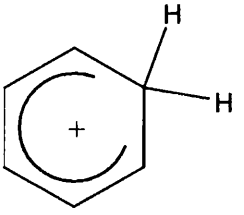

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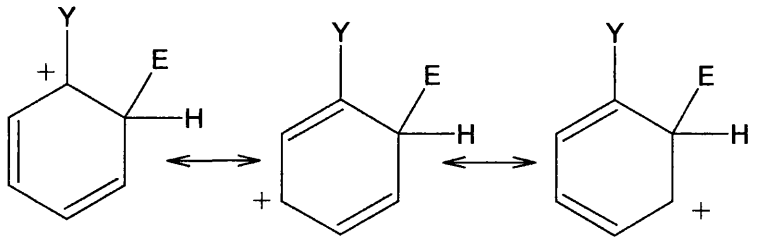
Figure 1.2: Structure of the benzenonium species (**4**) observed by low temperature carbon nuclear magnetic spectroscopy.

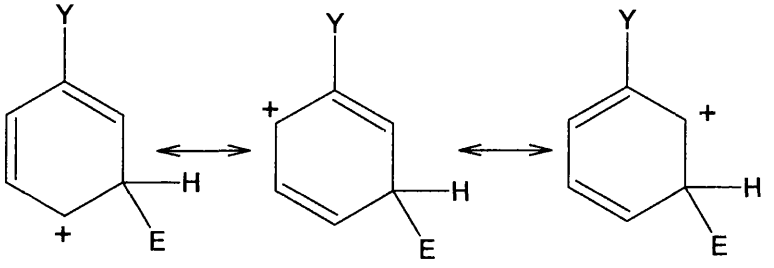
For monosubstituted benzene, substitution may be directed to the *ortho*, *meta*, or *para* position depending on the group already present on the ring, more precisely the inductive nature (field effects) and resonance effects which are introduced by the group.

The group also affects the rate of the reaction. Those that increase the rate relative to benzene are termed activating. Groups that decrease the rate relative to benzene are termed deactivating.

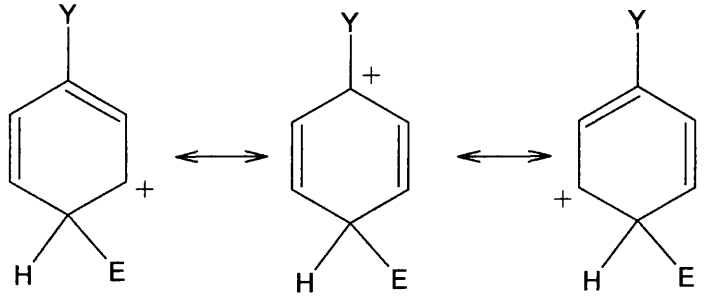
The effect a group will have can be predicted by looking at the theoretical arenium ions formed after electrophilic attack at the *ortho*, *meta* or *para* positions. (Schemes 1.4-1.6)



Scheme 1.4: *ortho*-Substituted arenium resonance diagram



Scheme 1.5: *meta*-Substituted arenium resonance diagram.



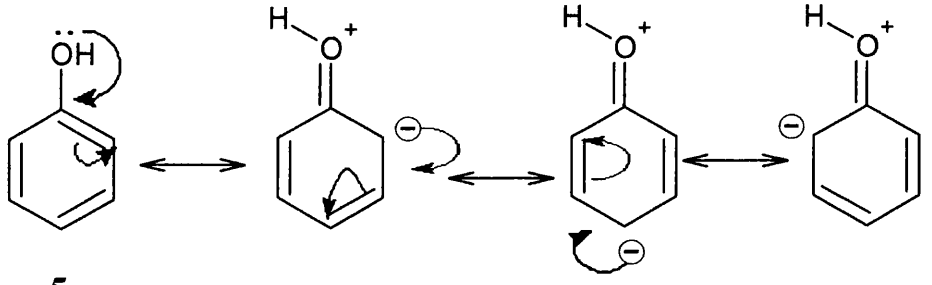
Scheme 1.6: *para*-Substituted arenium resonance diagram

Field effects occur due to differences in electronegativity between the substituent Y and the aromatic ring. Therefore, if the substituent is a more electronegative atom, such as oxygen, then it will attract some electron density away from the aromatic ring, and thus affect stability and reactivity.

Like the analogous arenium ions derived from benzene the ring has a positive charge, therefore any group with an electron donating field effect will stabilise the intermediate. Groups with electron withdrawing field effects will therefore destabilize the intermediate.

Field effects get weaker further away from Y, therefore have greater effect at carbon 1, then 2 and 6 *etc.* As can be seen from the canonical forms, only *ortho* and *para* substitution results in a positive charge on carbon 1, therefore a group with electron donating effect will stabilise the arenium ion resulting from attack at the *ortho* and the *para* positions more than the *meta*, and be *ortho*, *para* directing. Conversely groups with electron withdrawing field effects will destabilise *ortho* and *para* more than the *meta* position and be *meta* directing.

For phenol (**5**), aniline or any other group with a non-bonding pair of electrons on the corresponding Y substituent, resonance has greater control of regioselectivity than field effects (Scheme 1.7).



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Scheme 1.7: Resonance diagrams of phenol (**5**) showing greater electron densities at the *ortho* and *para* positions.

As can be seen from the canonical forms the *para* and *ortho* positions have the greatest share of electrons and therefore are more susceptible to electrophilic attack. Thus, the hydroxyl group and the majority of other groups with a lone pair on the atom attached to the ring are therefore *ortho-para* directing.

1.2.1 Substitution in disubstituted or polysubstituted rings.

More than one substituient on the ring presents a further complication to predicting the products of substitution, due to competition. However quite often groups present on the ring reinforce each other, as with *m*-cresol (**6**, Figure 1.3).

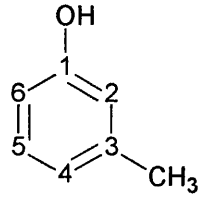

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Figure 1.3: An example of the directing substituents reinforcing each other in a disubstituted ring; in this case *m*-cresol (**6**)

The hydroxyl group is *para* and *ortho* directing, therefore the 2,6-(*ortho)* and 4-(*para*) positions are the most susceptible to substitution. The methyl group is also *para* and *ortho* directing, therefore the 2,4-(*ortho* to the methyl) and 6 (*para* to the methyl) positions are once again most susceptible to substitution. However, a rule (the *meta* rule) predicts that a substitution is less likely to occur between two groups with a *meta* relationship, therefore substitution at the 2-position is less favourable than the 4- and 6- positions. This type of reinforcement is not always the case, for example with *o*-cresol. (**7**, Figure 1.4)

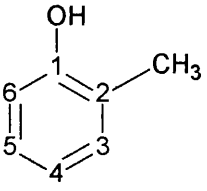

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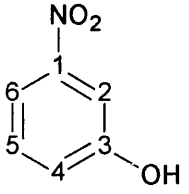
Figure 1.4: An example of the directing substituents competing with each other in a disbustituted ring; in this case *o*-cresol (**7**)

In this case the hydroxyl group promotes substitution at the 6 and the 4 positions, but the methyl group promotes substitution at the 3 and 5 position. The

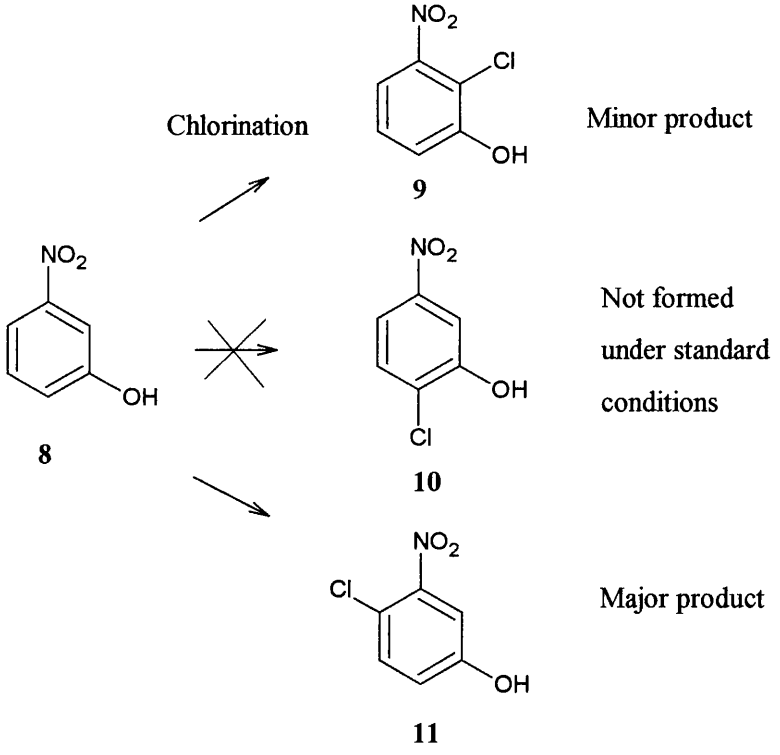
methyl group does not inhibit substitution at the groups *meta* to itself (6 and 4), but just promotes less at the *meta* relative to the *ortho* and *para* positions. So in theory all substitutions, 6, 5, 4 and 3 are possible, but in this type of ring system a second rule states that substitution tends to occur in accordance to the directing effects of the most activating group, in this case the hydroxyl group. Therefore the 6,4-substitutions will be expected to dominate.

A third rule in predicting the substitution product is known as the '*ortho* rule' which applies when there is an activating (*ortho*, *para* directing) group *meta* to a deactivating (*meta* directing) group, for example 3-nitrophenol. (**8**, Figure 1.5).



8

Figure 1.5: An example of a compound, 3-nitrophenol (**8**), that undergoes substitution obeying the *ortho* rule.

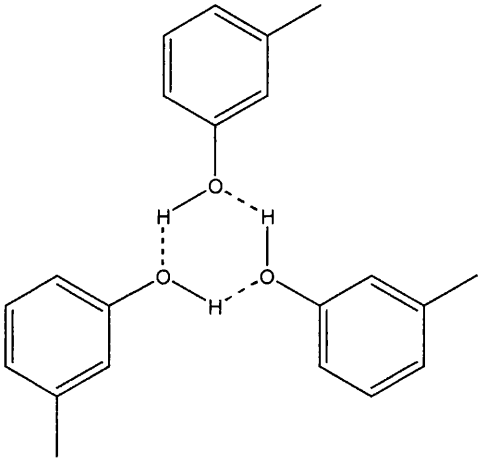


Scheme 1.8: Example of the *ortho* rule.

The *ortho* rule states that substitution occurs *ortho* to the *meta* directing group. To obey this rule chlorination occurs *ortho* to the nitro group, which gives two possibilities; a minor product (**9**) in accordance with the *meta* rule and a major product (**11**) by default (Scheme 1.8).

1.2.2 The *para*:*ortho* ratio

As defined by the principles above it is clear that there are few purely *ortho*, or purely *para* directing monosubstituted rings, and therefore the issue of regioselectivity is encountered time and again. As chlorinated aromatics are used on a large scale in industry, and specific regioisomers are needed for certain commercial products or for formation of certain fine chemicals, great effort has been undertaken to control or influence the *para*:*ortho* ratio. Statistically of course, for a monosubstituted benzene the ratio is expected to be 33:66 as there are two *ortho* positions and only one *para* position, but realistically the ratio can be influenced by various factors. Also, some substrates can exhibit very high *ortho* selectivity under certain conditions,[7] but very high *para* selectivity under different conditions.[8,9] Specific examples will be discussed in Section 1.4. Furthermore, the statistical pattern is different when the ring has more than one substituent. In the case of phenols, hydrogen bonding of the hydroxyl groups needs to be taken into account. For example, Bois reported that at low temperatures using x-ray crystallography *meta*-cresol exists as a trimeric structure with interaction of the individual units through hydrogen bonds at the hydroxyl groups (Scheme 1.9).[10] Such hydrogen bonding interactions may be effective in exposing the *para* position more then the *ortho* positions and hence increase the theoretical *para*:*ortho* ratio.



Scheme 1.9: Hydrogen bonding in *m*-cresol as observed by x-ray crystallography.

One of the most effective methods of influencing the *para*:*ortho* ratio to obtain the desired regioisomer is to control the steric factors influencing substitution, and this has been done by many ways, such as-

-Increasing or decreasing the bulkiness of the substrate or the electrophile.

-The use of shape selective reagents, i.e. zeolites, cyclodextrins or 'molecular clips' (molecules designed to generate specific spatial interactions to increase the regioselectivity of the reaction).

-The use of solid supports, such as silica.

-The use of spatially selective chlorinating agents that interact with the hydroxyl group through hydrogen bonding, resulting in the chlorine atom being in the vicinity of the *ortho* or *para* position.

These approaches, amongst others are discussed further in Section 1.4.

1.3 The use of chlorinated phenols

For a synthetic green chemist it is imperative to have an understanding of the industrial importance of the target molecules. In this case the desired products are specific isomers of chlorinated phenols, which are renowned for having a wide and diverse use in the chemical industry. Examples of such uses are briefly elaborated on in this section.

1.3.1 Chlorinated phenols as antibacterial agents

Phenols have been used as antibacterial agents since the 1860's, when Kuchenmeister used a phenolic solution derived from coal tar as a wound dressing, and Joseph Lister utilised the antibacterial activity of phenol as a spray and as an antiseptic for surgery.[11] Many simple phenols, cresols, xylenols and chlorinated phenols also act as antibacterial agents and disinfectants.

The relative ability of the phenols to act as effective antibacterial agents can be maximised by having an alkyl group at the *ortho* position and a halogen at the *para* position.[12] Some of the chlorinated phenols most widely used as antibacterial

agents[11, 12,13] (Figure 1.6) are: 2,4,6-trichlorophenol (**12**), used in formulated antiseptics such as TCP; 4-chloro-3,5-dimethylphenol (**13**, PCMX), which is a widely used disinfectant commercially known as Dettol; 2,4-dichloro-3,5-dimethylphenol (**14**, DCMX), which has properties similar to PCMX and is used in various formulated disinfectants such as pine disinfectants; 4-chloro-3-methylphenol (**15**), which is used as a preservative in the pharmaceutical industry; 4-chloro-2-phenylphenol (**16**) and 2-benzyl-4-chlorophenol (**17**), which also have good antibacterial properties and are used in commercial formulations.

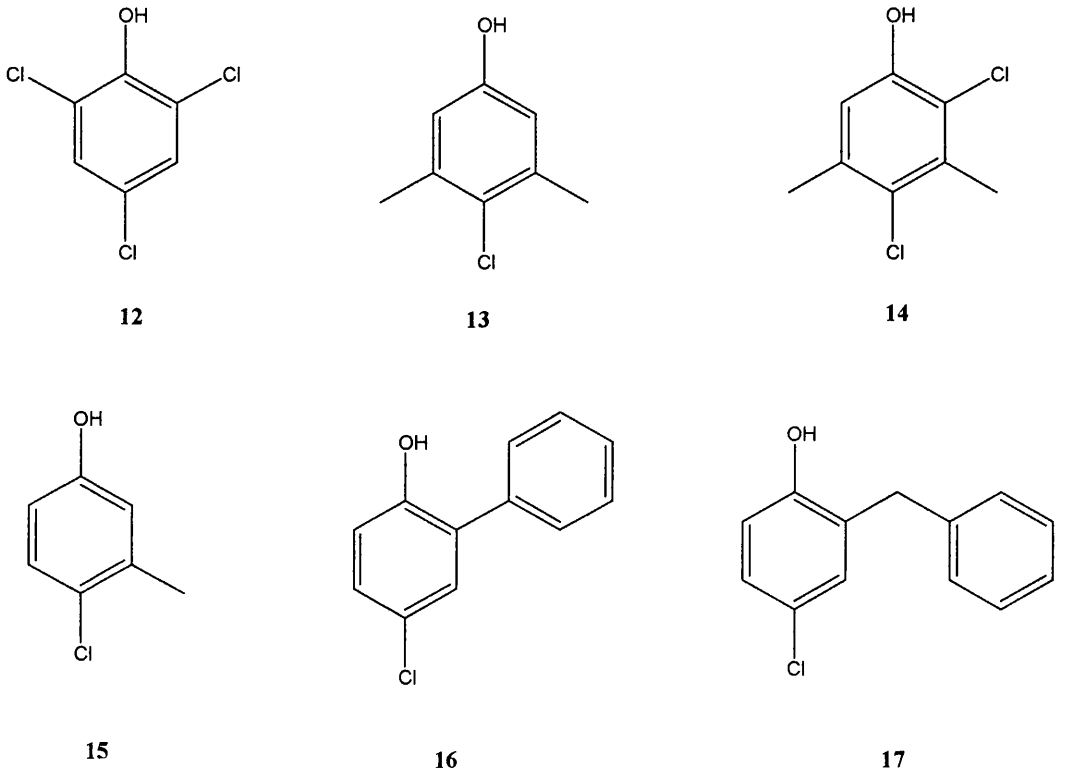
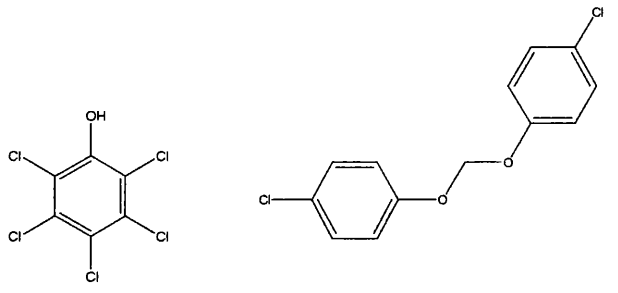


Figure 1.6: Some examples of chlorinated phenolic antibacterial agents.

1.3.2 Chlorinated phenols as herbicides, pesticides and fungicides.

Chlorinated phenols and their derivatives are not limited to their interaction with micro-organisms, as they are also functional as herbicides, pesticides and fungicides. For example, pentachlorophenol (**18**) has been widely used as an herbicide in rice fields[13] and dichlorophenoxymethane (**19**, DCPM) is an important *p*-chlorophenol derivative used as an insecticide replacement for DDT (Figure 1.7).[14] 4-Chloro-2-phenylphenol (**16**) is functional as an antibacterial, but is more widely

used as a fungicide.[12] 2,4,6-Trichlorophenol (**12**) has also been used as a fungicide and an insecticide.[15]

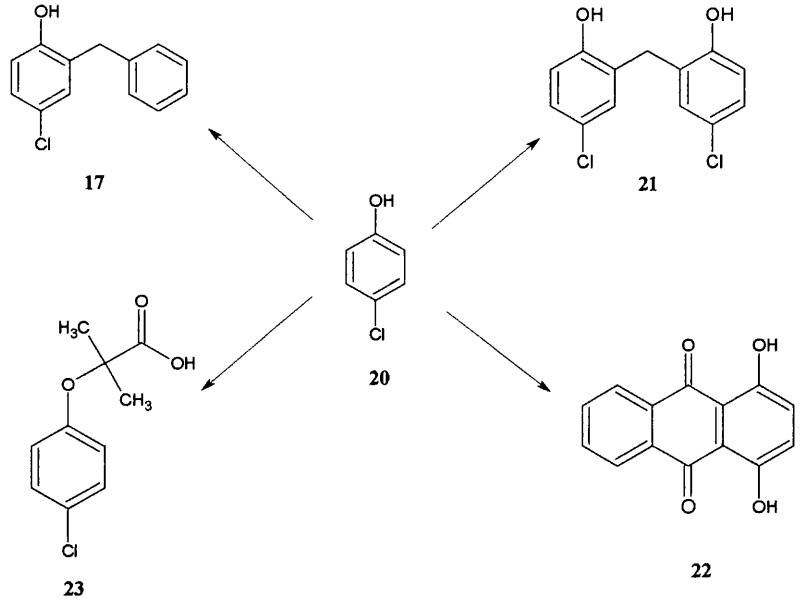


18 **19**

Figure 1.7: Pentachlorophenol (**18**) herbicide and dichlorophenoxymethane (**19**) insecticide.

1.3.3 Chlorinated phenols as important synthetic chemicals in industrial processes.

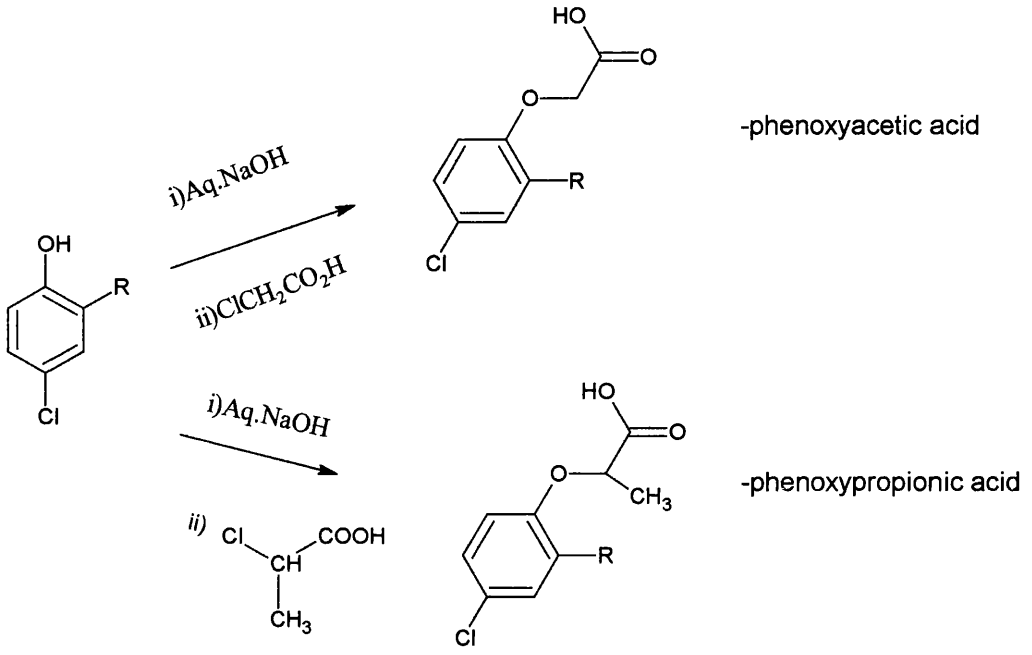
Chlorinated phenols are widely used as starting materials for the manufacture of industrially important chemicals (Scheme 1.10). 4-Chlorophenol (**20**) is a very important starting material for various industrial synthetic processes. For example it is used for the synthesis of the antibacterial agent 2-benzyl-4-chlorophenol (**17**);[16] the fungicide dichlorophen (**21**);[17] anthraquinone dyes such as **22**;[18] and the cholesterol reducing drug 2-(4-chlorophenoxy)-2-methylpropanoic acid (**23**).[19]



17 **21** **20** **22** **23**

Scheme 1.10: Some examples of industrially important compounds derived from 4-chlorophenol (**20**).

However, probably the most significant use of chlorinated phenols, is as starting materials for the manufacture of phenoxyacetic and phenoxypropionic acid derivatives (Scheme 1.11).



Where R = CH_3 or Cl.

Scheme: 1.11 Synthesis of phenoxyacetic and phenoxypropionic acids from chlorophenols.

Conversion of the phenol into the phenoxycarboxylic acid derivative proceeds via Williamson base catalysed ether formation.[20] The products are selective herbicides used for broad leaved plants, which work by mimicking indole acetic acid, which is an auxin regulator. The presence of the herbicide causes the plant to over grow and subsequently die from insufficient quantities of nutrients.[14]

For the phenoxyacetic acid products, when R = CH_3, 2-methyl-4-chlorophenoxyacetic acid (MCPA) is formed, while when R = Cl, 2,4-dichlorophenoxyacetic acid (2,4-D) is produced.[21] For the phenoxypropionic acid products, when R = CH_3, 2-(4-chloro-2-methylphenoxy)propanoic acid is the product. While when R = Cl, 2-(2,4-dichlorophenoxy)propanoic acid is the product. These compounds have similar property to the previous phenoxyacetic acid herbicides, but are more effective against chickweed and cereals.[22]

Another compound analogous to these herbicides above is 2,4,5-trichlorophenoxyacetic acid (**24**, Figure 1.8), which is used for selective weed control in conifers.[23]

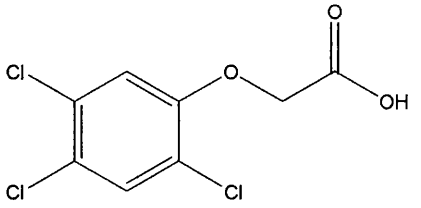


Figure 1.8: Herbicide 2,4,5-trichlorophenoxyacetic acid (**24**).

As illustrated above chlorinated phenols have a wide role in industrial synthesis, and in every aromatic substitution (chlorination step) there is a significant quantity of unwanted isomers formed. This is an undesirable situation in terms of green chemistry and in terms of the economical factors related to production. For both these reasons a significant amount of investigation has been undertaken to obtain a more selective chlorination system for phenols.

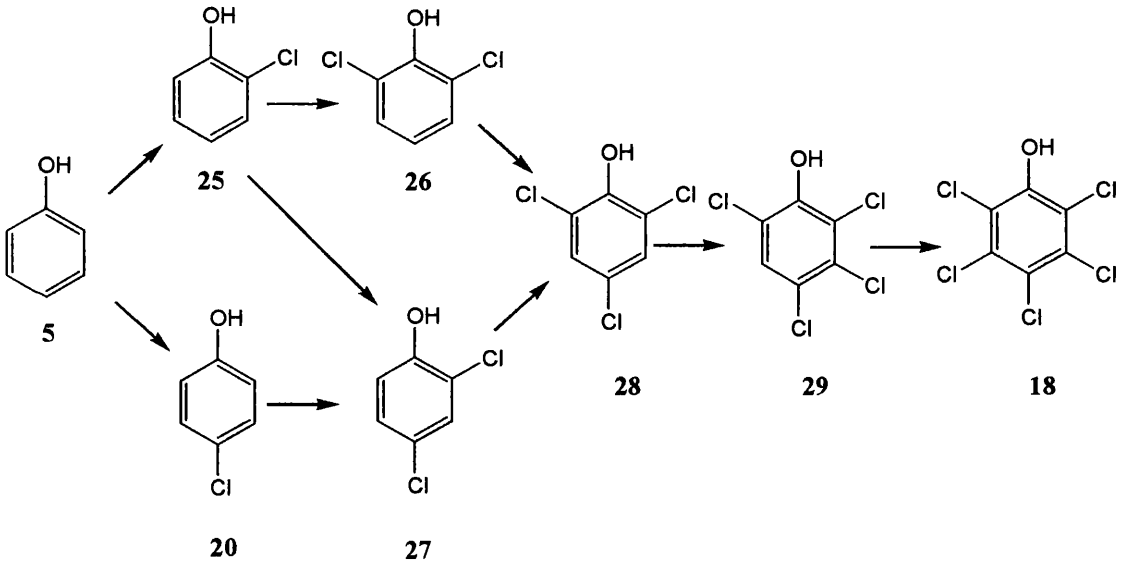
1.4 A general review of previous chlorination methods employed.

1.4.1 Chlorination systems.

It is more accurate to discuss chlorination methods by comparing different 'systems' of chlorination, rather than just comparing different chlorinating agents. This is because the combination of the chlorinating agent, catalyst, co-catalyst, solvent, solid supports and physical conditions are all fundamentally important, and individual factors are not necessarily inter-changeable within different system.

1.4.2 Molecular chlorine systems.

Molecular chlorine is a cheap and widely available gas. Molecular chlorine acts as a strong electrophile, and being diatomic is a relatively small compound. This combination makes it very useful for the polychlorination of activated aromatics (Scheme 1.12).

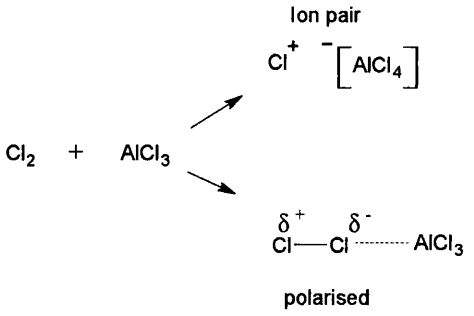


Scheme1.12: Polychlorination of phenol (**5**).

The rates of monochlorination and dichlorination of phenol are similar and even the trichloro product (**28**) can be formed early on in the reaction.[7a] As the melting and boiling points of these products are similar it is very difficult to isolate any particular component in high yield. For example, the maximum yield of 4-chlorophenol (**20**) is 49 %.

Tetrachlorophenols and pentachlorophenol (**18**)[2b] were initially the desired industrial products, particularly the pentachlorophenol. The mono-, di- and tri-chlorophenols where obtained readily using molecular chlorine, but further chlorination required the use of a catalyst such as $FeCl_3$,[2d, 2a, 24] $AlCl_3$, [2a, 2d] $SbCl_5$,[2d] $SbCl_3$,[2c] $TeCl_4$,[25] or iodine.[2d]

Lewis acids have classically been used to increase the electrophilic ability of molecular chlorine as a reagent and the interaction is frequently represented by the polarisation of chlorine or by the formation of an ion pair (Scheme 1.13). The polarising ability of Lewis acids towards electrophiles has been frequently utilised for the substitution of less reactive aromatics such as benzene.



Scheme1.13: Interaction of $AlCl_3$ with molecular chlorine.

From the1930s to the 1950s the demand for pentachlorophenol was diminishing relative to the increasing demand for mono and disubstituted products. Particular emphasis was on the formation of *para*-chloro-*meta*-xylenol (**13**, PCMX, Dettol),[26] monochlorocresols[2e] and dichlorocresols.[2f]

The best *para*:*ortho* ratio obtained on chlorination of phenol with molecular chlorine is 6.4 which proceeds *via* a borate ester[27] by the use of boric acid as a catalyst in chloroform. Boric acid was easily recycled, but the *para*:*ortho* ratio is low compared to other chlorinating systems.

The most regioselective system using molecular chlorine to chlorinate phenols involves the use of acetic acid anhydride, where only the *ortho* product is obtained. Initially the chlorine reacts with the anhydride to form acetyl chloride, which interacts with phenol in such a way that the chlorine on acetyl chloride is in the proximity of the *ortho* position (Figure 1.9).[28]

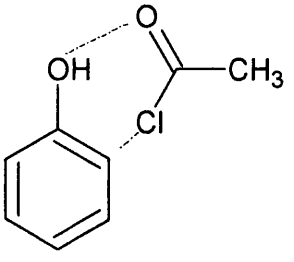


Figure 1.9: The interaction of acetyl chloride with phenol resulting in *ortho* chlorination.

The interaction shown in Figure 1.9 represents the interaction prior to the chlorination. It is clear that the chlorine atom on the acetyl chloride can not interact at the *para* position, resulting in a high yield of the *ortho* product. Except for this

example, chlorination using molecular chlorine is very difficult to control selectively. This coupled with the increased demand for mono and dichloro products prompted the investigation of other chlorinating agents, particularly milder chlorinating agents having the ability to monochlorinate or dichlorinate phenols.

In addition to poor selectivity another disadvantage of molecular chlorine is poor control of stoichiometry, as bubbling a gas into a reaction vessel is difficult to account for in quantitatively accurate manner. Molecular chlorine is also a notorious toxic gas previously used for military purposes, and the use of such a chemical on a large scale is a significant hazard.

Attempts have been made to produce reagents that react analogously to molecular chlorine but without the hazards associated with chlorine gas. Tin (IV) chloride and lead tetraacetate acts as a safe source of molecular chlorine in solution (Scheme 1.14).[29]

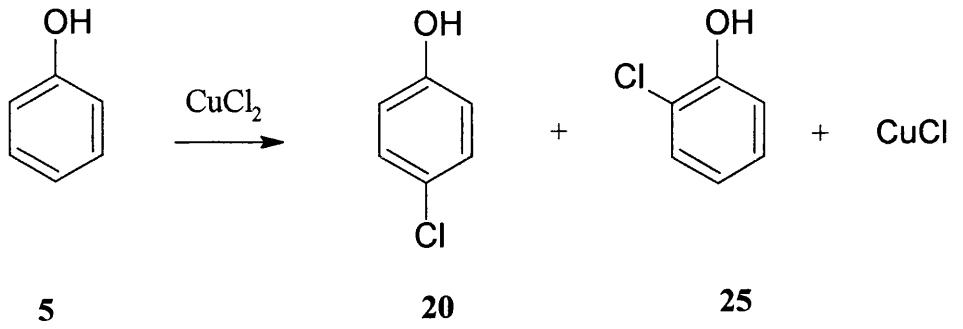
$$2\ SnCl_4 \quad + \quad Pb(OAc)_4 \quad \longrightarrow \quad Cl_2 \quad + \quad 2\ Cl_3SnOAc \quad + \quad Pb(OAc)_2$$

Scheme1.14: The in situ generation of molecular chlorine from tin chloride and lead tetraacetate.

There are fewer problems with handling and stoichiometry associated with this precursor method. However, it results in a large amount of heavy metal waste and is therefore not attractive form a green chemistry perspective.

1.4.3 Copper (II) chloride systems

$CuCl_2$ has been used for the chlorination of phenols and proceeds via the reduction of the copper (II) species (Scheme 1.15). The success of the chlorination is strongly dependent on the choice of other reagents. Two main reactions have been studied, the first involving the use of a non-polar solvent where copper (II) chloride is not dissolved, and therefore chlorination occurs heterogeneously,[30] and the second in acidic or basic conditions where the copper (II) chloride is in solution[31] and chlorination occurs homogeneously. The copper (I) chloride formed has been found to reduce the efficiency of the chlorination under homogenous conditions only.



5 **20** **25**

Scheme 1.15: Copper (II) chloride chlorination of phenol (**5**) and formation of copper (I) chloride.

Copper (II) chloride has been investigated with a range of Lewis acid co-catalysts with varied success. The Lewis acids that do increase the rate of chlorination, such as aluminium, beryllium, and chromium halides have been believed to operate via a 1:1 complex with the copper salts.[32]

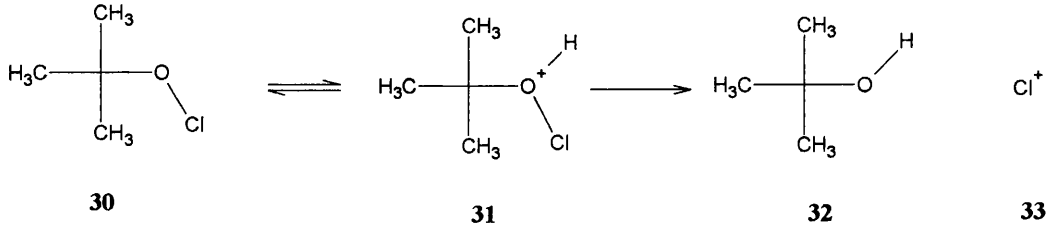
The best *para*:*ortho* ratio obtained for the reaction of phenol with copper (II) chloride is around 14, in concentrated hydrochloric acid in the presence of oxygen. The active species for the chlorination is believed to be H_2CuCl_4 which is formed in the presence of hydrochloric acid. The role of oxygen is to regenerate the copper (II) species. The use of copper (II) chloride is attractive economically due to its availability and price.

1.4.4 *tertiary*-Butyl hypochlorite systems

It was originally believed that the use of *t*-butyl hypochlorite (**30**) was efficient at producing relatively high *ortho*:*para* ratios. Extensive work by Harvey and Norman scrutinised and re-interpreted practically all previous results of the chlorination using *t*-butyl hypochlorite.[33]

Harvey and Norman presented some very interesting results to confirm their initial speculation for the function of *t*-butyl hypochlorite as a chlorinating agent. They suggested that the regioisomers produced from the use of *t*-butyl hypochlorite could be explained in terms of the active chlorinating species generated under certain conditions.

In acid conditions the *t*-butyl hypochlorite is readily protonated, the oxonium species generated (**31**) breaks down to the corresponding alcohol (**32**) and the active chlorinating species, the chlorinium ion (**33**, Scheme 1.16).



30 **31** **32** **33**

Scheme 1.16: Generation of chlorinium ion from *t*-butyl hypochlorite.

Therefore when *t*-butyl hypochlorite (**30**) was exposed to acidic conditions the *ortho*: *para* ratio should be similar to that obtained by the use of the chlorinium ion, which was found to be the case. Chlorinium ion in water, and *t*-butyl hypochlorite in sulfuric acid both gave an *ortho*:*para* ratio of around 1:1 in the chlorination of phenol. Phenol itself is sufficiently acidic to produce the chlorinium ion in solution.

In neutral conditions *t*-butyl hypochlorite produced the same ratio of isomers as molecular chlorine and this was rationalised by the assumption that it is very likely that the chlorinating species in both cases are the same and that *t*-butyl hypochlorite decomposes to produce molecular chorine in solution.[32]

Under alkaline conditions the phenol readily forms the phenoxide anion and the *t*-butyl hypochlorite is hydrolysed to hypochlorous acid. Under these conditions, for example in the presence of sodium hydroxide, then an *ortho*:*para* ratio of around 4:1 is attainable, which is equivalent to that obtained by hypochlorous acid in water alone, indicating that the active chlorinating species is the same in both cases. The relatively high *ortho*:*para* ratio is believed to be formed in an analogous way to that when acetyl chloride and molecular chlorine are used (Figure 1.10, see also Section 1.4.2).

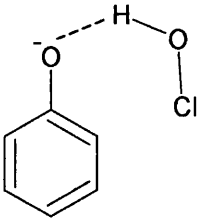


Figure 1.10: Interaction of hypochlorous acid with phenol leading to a high *ortho*:*para* selectivity.

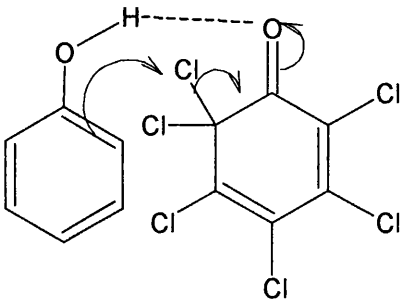
The result of the hydrogen bonding is to bring the chlorine into the proximity of the *ortho* position, and therefore it is more likely to react at the *ortho* position.

Despite the fact that *t*-butyl hypochlorite is not believed to be the active chlorinating agent under basic, acidic or even neutral conditions its ability to act as a precursor for reactive chlorinating agents coupled with the fact it is cheaply and easily formed, makes it a useful reagent for the chlorination of aromatics. *t*-Butyl hypochlorite has been investigated as a chlorinating agent in the presence of solid supports such as silica and zeolites.[34] These systems provide good selectivity for certain aromatics but no significant results for phenols.

Hypochlorous acid has been used as a chlorinating agent in the presence of shape selective cyclodextrins. The cyclodextrins were efficient at selectively *para* chlorinating anisole, but at *ortho* chlorinating cresols.[35]

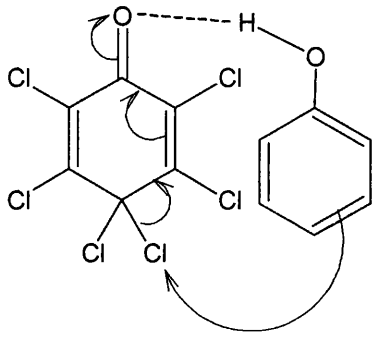
1.4.5 Polychlorinated cyclohexadienone systems.

Polychlorinated cyclohexadienones (**34**, **35**) have been synthesised from pentachlorophenol and molecular chlorine and interact with phenol as shown in Schemes 1.17 and 1.18. Once again the ability for the hydroxyl group to interact through hydrogen bonding with electronegative atoms is utilised.



34

Scheme 1.17: *ortho*-Specific interaction of phenol with a polychlorinated cyclohexadienone species (**34**).



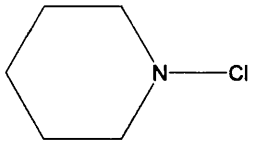
35

Scheme 1.18: *para*-Specific interaction of phenol with a polychlorinated cyclohexadienone species (**35**).

2,3,4,5,6,6-Hexachlorocyclohexa-2,4-dien-1-one (**34**) undergoes hydrogen bonding with phenol and generates a spatial arrangement which brings the reactive chlorine in the proximity of the *ortho* positions. Similarly, 2,3,4,4,5,6-hexachlorocyclohexa-2,5-dien-1-one (**35**) hydrogen bonds with phenol but this time generates a spatial arrangement which brings the reactive chlorine in the proximity of the *para*-position[36] These polychlorinated cyclohexadienones can therefore be used to produce a high *para*:*ortho* ratio and/or a high *ortho*:*para* ratio respectively. These compounds have also been used to chlorinate naphthols in an analogous fashion, but isolated yields in both cases are generally low.[37]

1.4.6 *N*-Chloroammonium salts and *N*-chlorodialkylamine systems.

Compounds of the type $(R_3N\text{-}Cl)^+$ and $R_2N\text{-}Cl$, common examples of which are shown in Figure 1.11, are successful in producing very high regioselectivity in the chlorination of activated aromatics in acidic solutions.[8]



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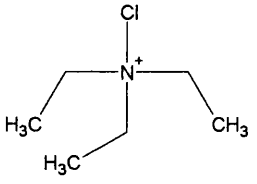


37

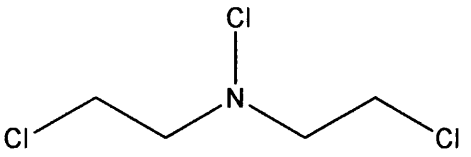
Figure 1.11: Examples of *para*-selective *N*-chlorocompounds.N-Chloropiperidine (**36**) and N-chlorotriethylammonium chloride (**37**)

N-Chloropiperidine (**36**) and N-chlorotriethylammonium chloride (**37**) are both highly regioselective chlorinating agents for phenol, and both give a *para*:*ortho* ratio of 32:1, with yields of monochlorophenol being 100 % and 98 % respectively. The reaction is acid dependent and is carried out in trifluoroacetic acid or in sulfuric acid. In sulfuric acid the selectivity increases with increasing acidity.

The high regioselectivity has been attributed to the bulk of the chlorinating species, which inevitably leads to chlorination at the more accessible reactive site being favoured, in this case the *para*-position as opposed to the *ortho*-position.

The use of strong acids in excess on an industrial scale is undesirable in terms of green chemistry. A replacement for the excess acid solution was investigated by means of using an acidic silica as a solid support.[7b] Surprisingly under these conditions the *ortho* product was the major product, though the exact reason for that

finding is unclear. Using other *N*-chlorodialkylamines *ortho:para* ratios as high as 16:1 were achieved using *N*-chlorobis(2-chloroethyl)amine (**38,** Figure 1.12) as the chlorinating agent.

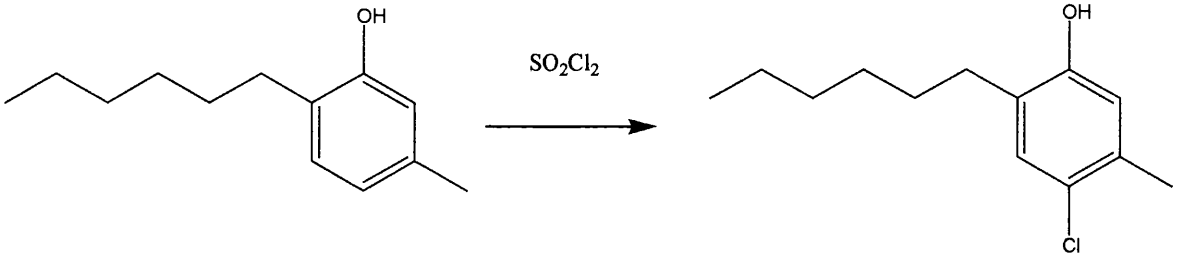


38

Figure 1.12: *N*-chlorobis(2-chloroethyl)amine (**38**).

1.4.7 Sulfuryl chloride systems.

Sulfuryl chloride is a weak, bulky electrophile relative to molecular chlorine,[38] for this reason it is more selective for monochloroination. Sulfuryl chloride was used to chlorinate phenols by Sah[39] in 1941. Sah monochlorinated 3-methyl-6-n-hexyl phenol (**39**) to form a bactericide 4-chloro-3-methyl-6-*n*-hexyl phenol (**40**) with a yield of 65 % (Scheme 1.19).



39 **40**

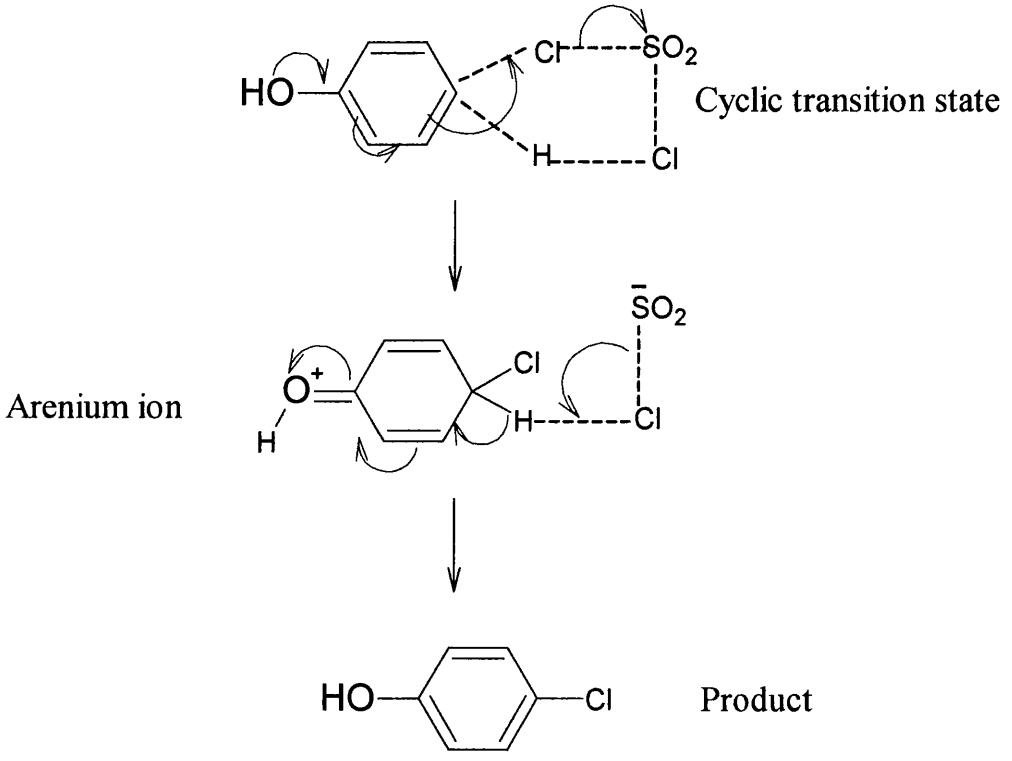
Scheme 1.19: Formation of bactericide (**40**) using sulfuryl chloride to chlorinate **39** at the *para*- position.

Quantitative analysis of the reaction products from the reaction of sulfuryl chloride with aromatic substrates shows that the reaction can be accurately expressed by the equation shown in Scheme 1.20.[38]

$$SO_2Cl_2 + ArH \longrightarrow ArCl + SO_2 + HCl$$

Scheme 1.20: Stoichiometric equation of the interaction of sulfuryl chloride with aromatic compounds.

Kinetic studies suggest that molecular sulfuryl chloride is the chlorinating species, and in the absence of a Lewis acid catalyst, chlorination proceeds via a cyclic transition state (Scheme 1.21).[38, 40]

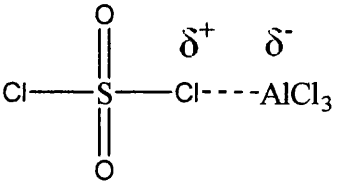


Scheme 1.21: Reaction of sulfuryl chloride with phenol *via* a 5 member cyclic transition state.

As can be seen from the cyclic transition state, the spatial arrangement of atoms represents a relatively large area and therefore its bulkiness should favour the *para*-position. This is the case as the direct reaction of sulfuryl chloride with *o*-cresol gives a *para*:*ortho* ratio of 6:1, whereas the direct reaction of molecular chlorine with *o*-cresol gives a *para*:*ortho* ratio in the region of 2:1.[41]

Kinetic studies also indicate that decomposition into SO_2 and Cl_2 has no effect on chlorination, and therefore does not occur in solution to any significant extent.[38]

Sulfuryl chloride forms a complex with Lewis acids, which is effective in increasing the *para* selectivity due to increased bulkiness of the chlorinating species, but does not significantly increase the rate of reaction.[42,7a] For example when $AlCl_3$ is used then complex **40** is formed (Figure 1.13).



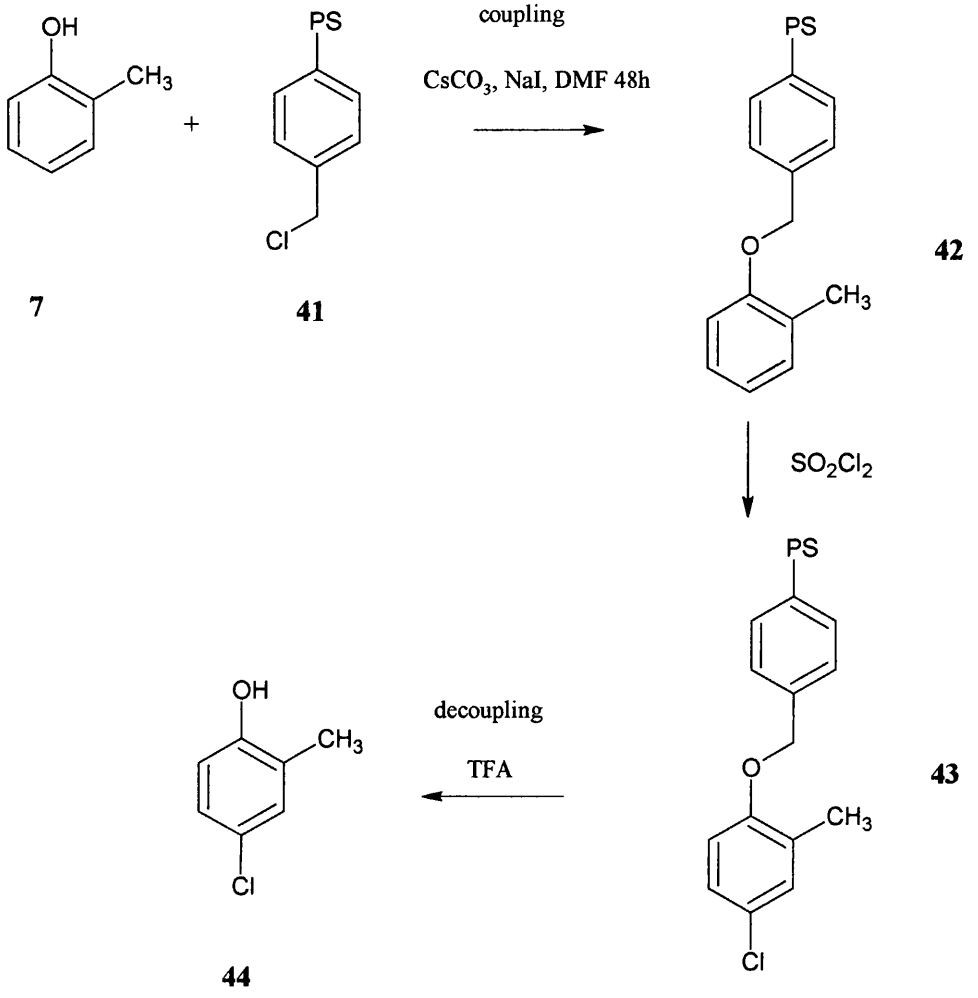
40

Figure 1.13: Aluminium chloride-sulfuryl chloride complex (**40**).

Early use of sulfuryl chloride with metal halides predominantly involved $FeCl_3$ which gave a *para*:*ortho* ratio of 11:1 for the reaction with phenol.[42] Later, $AlCl_3$ was more commonly used, presumably because it was cheaper and generally more *para* selective.[43] Sulfuryl chloride has also been used in the presence of zeolites but has shown no significant selectivity in the reactions with phenols.[44]

Sulfuryl chloride can also be used for highly regioselective *ortho*-chlorination, by using amines as catalysts. Sulfuryl chloride catalysed with di-*iso*-butylamine gives a 91 % yield of the *ortho* product and an *ortho*:*para* ratio of 22:1. By using almost stoichiometric amounts of amine, as opposed to catalytic amounts, an *ortho*:*para* ratio of 66:1 can be achieved, but with a reduction in yield to 79 %. Also, this latter method gives a significant amount of undesirable polychlorinated phenols persistently.[45]

Modified Merrifield resins have been used to influence the nature of the substrate to enhance regioselectivity (Scheme 1.22).[9a]



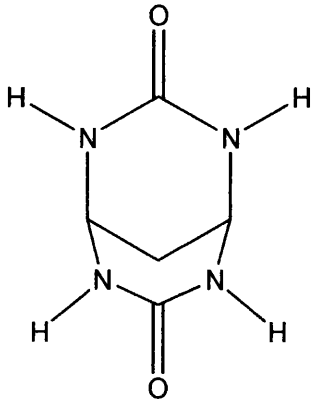
7 41 42 43 44

Scheme 1.22: *para*-Selective chlorination of *o*-cresol by the coupling and decoupling with a Merrifield resin.

The Merrifield linked *o*-cresol (**42**) is chlorinated highly selectively in favour of the *para*-product with a *para*:*ortho* ratio in excess of 50:1, which arises due to steric and electronic factors. This procedure has many advantages compared to other chlorination methods used, for example no requirement for Lewis acid and easy removal of the Merrifield resin, but unfortunately small amounts of the undesirable dichloro-cresol products are obtained consistently, solvent is required in the chlorination step, and the procedure requires three distinct steps, which has obvious disadvantages over commercially desirable 'one pot synthesis.'

Sulfuryl chloride has also been used in the presence of shape selective substrates designed to allow interaction at the *para*-position but sterically hinder substitution at the *ortho*-position. 'Molecular clips' derived from

2,4,6,8-tetraazabicyclo[3.3.1]nonane-3,7-dione (**45**, Figure 1.14) have been used in the sulfuryl chloride chlorination of *o*-cresol.[46]



45

Figure 1.14: 2,4,6,8-Tetraazabicyclo[3.3.1]nonane-3,7-dione (**45**) used to synthesise shape selective 'molecular clips'.

When these shape selective molecules derived from **45** are used in near stoichiometric amounts (0.9 mole equivalents) it results in a high *para*-selectivity with a *para*:*ortho* ratio of around 25:1. However when catalytic amounts of this expensive catalyst are used the selectivity is considerably lower.

Sulfuryl chloride has also been used in conjunction with sulfide catalysts. This method is the most significant in terms of the work presented in this thesis and is discussed separately in Section 1.6.

1.5 Green Chemistry considerations

Over the last 20 years there has been increasing awareness of our own ability to harm our world, with particular emphasis on our contribution to global warming, ozone depletion, bioaccumulation and atmospheric pollution. This awareness has led to the birth of various strategies designed to reduce the potential damage these problems can impact. One such strategy is known as 'green chemistry' which operates at the root of the problem, and can be defined as the design, development and

implementation of chemical or chemical products or processes to reduce or eliminate the use and generation of hazardous and toxic substances.

1.5.1 The 12 principles of Green Chemistry[47]

Green chemistry has been represented by 12 principles put forward by Anastas and Warner. The incorporation of these principles into traditional and new synthetic processes is the main objective of the modern day green chemist. A brief description of the 12 principles is listed below.

1-Prevention- it is better to prevent waste than to treat or clean up waste after it has been created.

2-Atom economy- synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3-Less hazardous chemical syntheses- wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4-Designing safer chemicals- chemical products should be designed to effect their desired function while minimising their toxicity.

5-Safer solvents and auxiliaries- the use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous.

6-Design for energy efficiency- energy requirements of chemical processes should be recognized for their environmental and economical impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.

7-Use of renewable feedstocks- a raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.

8-Reduce derivatives- unnecessary derivatization should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.

9-Catalysis- catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10-Design for degradation- chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.

11-Real-time analysis for pollution prevention- analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12-Accident prevention- substances and the form of substances in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

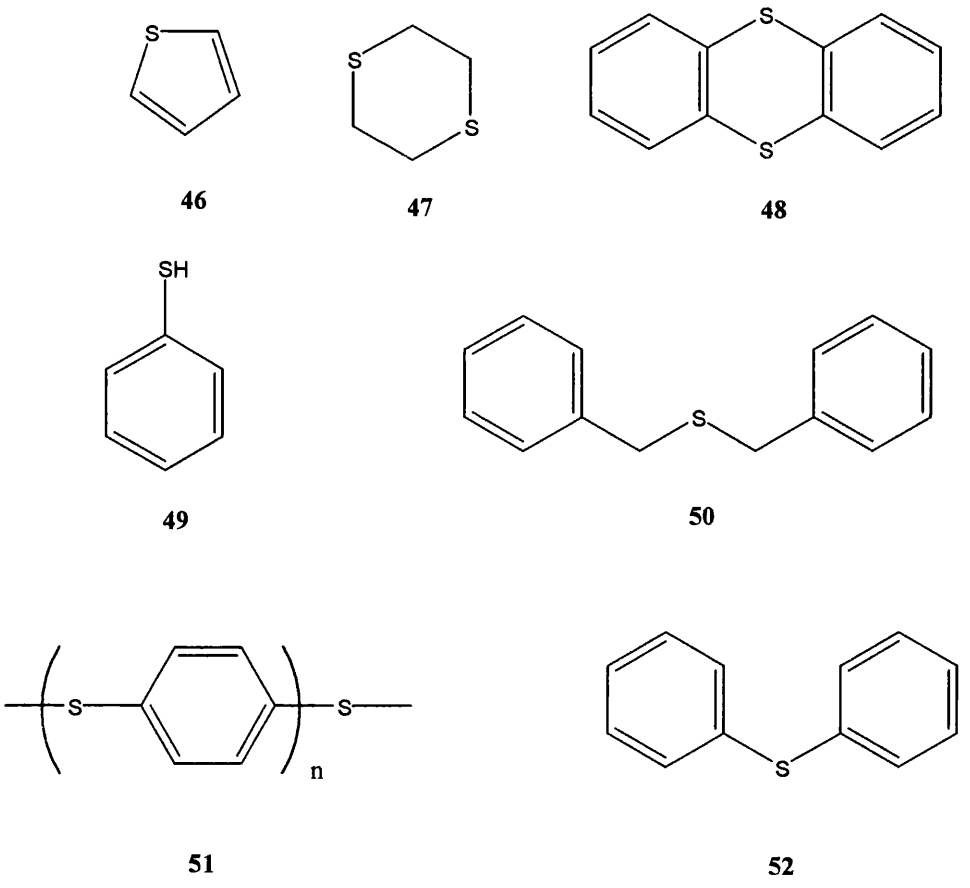
1.5.2 Green analysis of literature chlorination systems.

In terms of a process for the mono-*para*-chlorination of phenols all the methods described above are without exception severely flawed from a green chemistry and an industrial chemistry perspective. The majority of systems can be instantly discarded due to low product selectivity (principle 1). Out of the few selective systems the hexachlorocyclohexadienones methods (see Section 1.4.5) are flawed because the isolated yields are low (principle 2). The selective *N*-chloroammonium salts and *N*-chlorodialkylamines method (see Section 1.4.6) require stoichiometric amounts of strong acids (principle 3). The selective method using modified Merrifiled resins (1.4.7) requires three distinct steps, which is uneconomical in terms of green and industrial chemistry (principle 8).

However, from the literature one methodology stands out and has significant appeal and high potential in terms of green chemistry. The method involves the selective chlorination of phenols with sulfuryl chloride in the presence of catalytic amounts of a sulfide containing catalyst.

1.6 Chlorination systems involving divalent sulfur compounds in the presence of sulfuryl chloride.

Sulfuryl chloride has been used in conjunction with divalent sulfur compounds. Watson has investigated various divalent sulfur compounds such as thiophene (**46**), *p*-dithiane (**47**), thianthrene (**48**), thiophenol (**49**), dibenzyl sulfide (**50**), poly(1,4-phenylenesulfide) (**51**), and diphenyl sulfide (**52**, Figure 1.15) [7a, 41, 48].



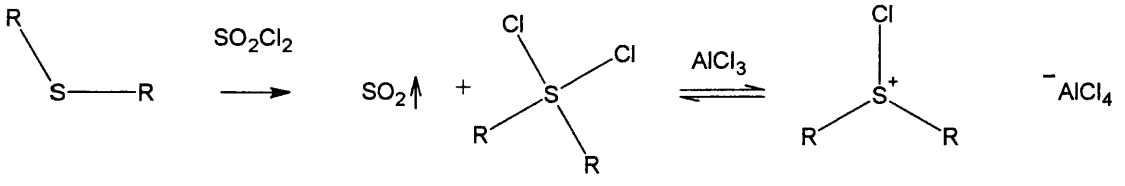
46 **47** **48**

49 **50**

51 **52**

Figure 1.15: Examples of sulfur compounds used as catalyst by Watson.

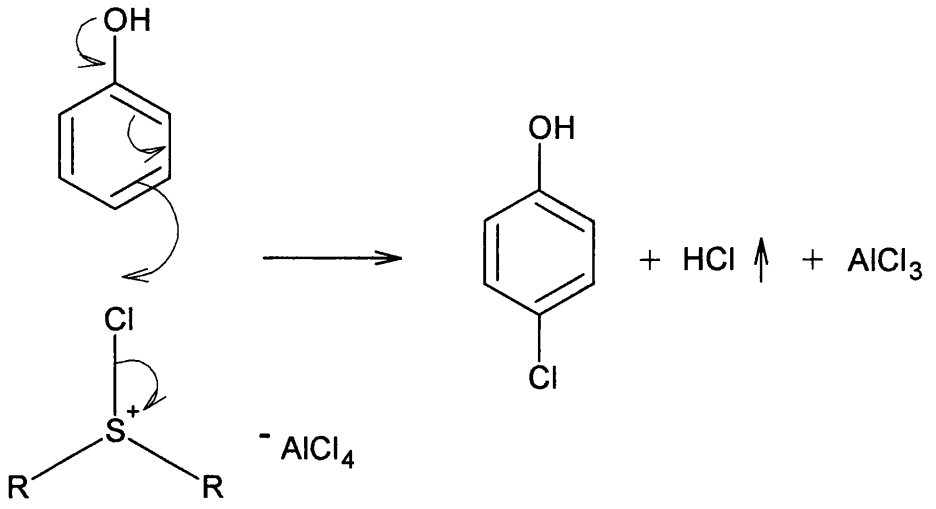
It is believed that divalent sulfur compounds interact with sulfuryl chloride to initially form a tetravalent sulfur intermediate (Scheme 1.23).



53

Scheme 1.23: Proposed formation of a chlorosulfonium species (**53**) believed to be the active chlorinating species when sulfuryl chloride, aluminium chloride and a sulfide catalyst are used for the chlorination of phenols.

In the presence of a Lewis acid this intermediate forms a trivalent sulfur intermediate (**53**) with a positive formal charge. This intermediate is the likely chlorinating species (Scheme 1.24).

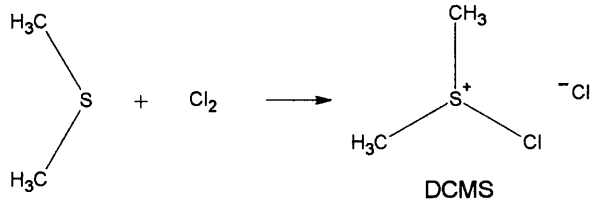


53

Scheme 1.24: The *para*-chlorination of phenol with the chlorosulfonium ion (**53**).

It is conceivable that the chlorine electrophile is attacked to regenerate the divalent sulfur species, and to form the arenium intermediate which eventually leads to the product and HCl evolution.

Compounds analogous to the trivalent sulfur intermediate can be isolated and are effective in the selective *para* chlorination of phenols. Olah[49] synthesised chlorodimethylsulfonium chloride (**54,** DCMS, Scheme 1.25).



54

Scheme 1.25: Formation of DCMS (**54**).

DCMS was used to chlorinate phenol and gave an 84 % yield of *p*-chlorophenol. No *ortho* product was determined, although it was probably present prior to purification. Diphenyl sulfide (**52**) has been investigated with the use of various metal halide/Lewis acid catalysts. Fe, Al, and Sb compounds prove to be the

most selective.[58] The combination of diphenyl sulfide and $AlCl_3$ to chlorinate *o*-cresol gives a yield of 94 % of the *para*-product and a *para*:*ortho* ratio of 18.8:1.[48]

Various other dialkyl sulfides have been investigated.[50] Dibutyl sulfide and diisiopropyl sulfide seemed the most promising and showed analogous results to diphenyl sulfide, but dialkyl sulfides tend to leave a sulforous stench even in trace amounts and can be difficult to separate from the reaction products. For these reasons it seemed desirable to investigate larger molecular weight sulfur compounds.

Dithiaalkanes of the type shown in Figure 1.16 have been synthesised.[51] The best *para*:*ortho* ratio of 20.7:1 was obtained with 5,18-dithiadocosane.

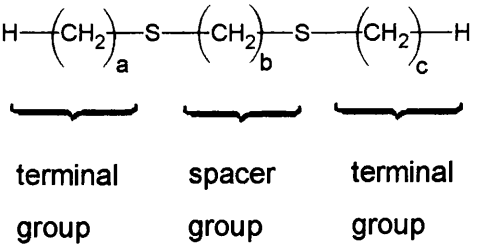


Figure 1.16: Generic representation of a dithiaalkane.

Modified Merrifield resins containing dithialkanes were also synthesised and gave good *para* selectivity of around 17. These heterogeneous reagents have the advantage of being easily separated from the crude product by simple filtration. Polythiaalkanes of the type shown in Figure 1.17 have also been synthesised.

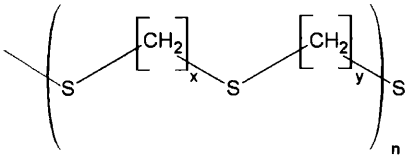


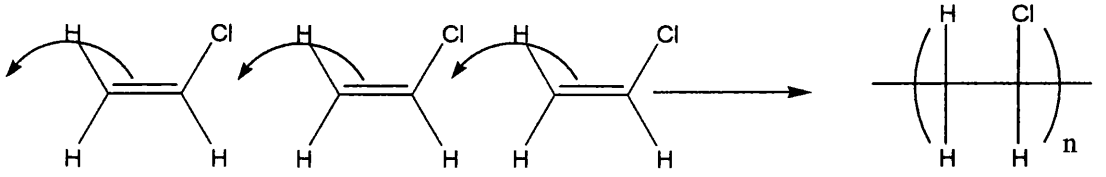
Figure 1.17: Generic representation of a polythiaalkane.

These polymers behave analogously to simple sulfides and therefore probably follow mechanisms like those shown in Scheme 1.23 and 1.24 and show excellent selectivity and potential for industrial application. The method has significant advantages in terms of green chemistry (see Section 1.5) over traditional chlorination procedures and is suitable for large scale synthesis.

This thesis will involve the synthesis of novel thiapolymers and the investigation of their application as catalysts for the chlorination of phenol, *o*-cresol, *m*-cresol and *m*-xylenol.

1.7 Aspects of polymer synthesis and characterisation

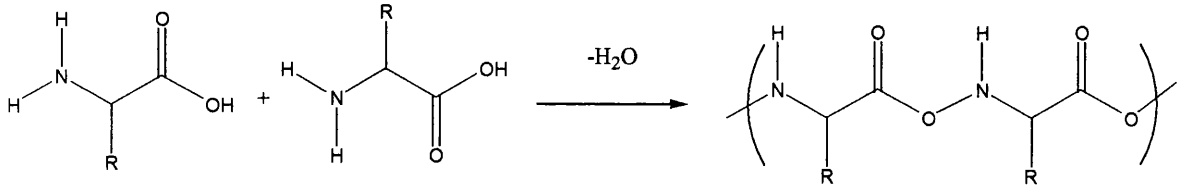
There are two major types of synthetic polymers- addition polymers and condensation polymers. Addition polymers are produced by the sequential addition of one molecule to a growing chain usually with a reactive intermediate such as a cation, anion or a radical at the end of the chain. The monomers are frequently alkenes and polymerisation in that example involves successive addition across the double bonds as shown in Scheme 1.26.



55 **56**

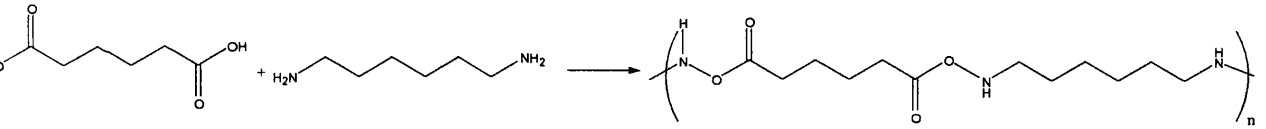
Scheme 1.26: Addition polymerisation of vinyl chloride (**55**) to synthesise PVC (**56**).

Condensation polymers result from condensation (bond formation with the loss of a small molecule) between monomers. The monomers are either a single bifunctional compound with two complementary groups such as the synthesis of polyamides from amino acids (see Scheme 1.27) or a pair of bifunctional compounds with two identical groups on the same monomer such as the condensation of adipic acid (**59**) and 1,6-diaminohexane (**60**) to synthesise Nylon 6,6 (**61**, Scheme 1.28).



57 **58**

Scheme 1.27: Condensation polymerisation of an amino acid (**57**) to synthesise a polyamide (**58**).



59 60 61

Scheme 1.28 Condensation polymerisation of adipic acid (**59**) and 1,6-diaminohexane (**60**) to synthesise Nylon 6,6 (**61**).

Common methods for the analysis of synthetic polymers include infrared spectroscopy,[52] NMR spectroscopy,[53] and HPLC.[54] Information about the molecular weight is often determined by GPC/SEC[55] and/or MALDI mass spectrometry.[56]

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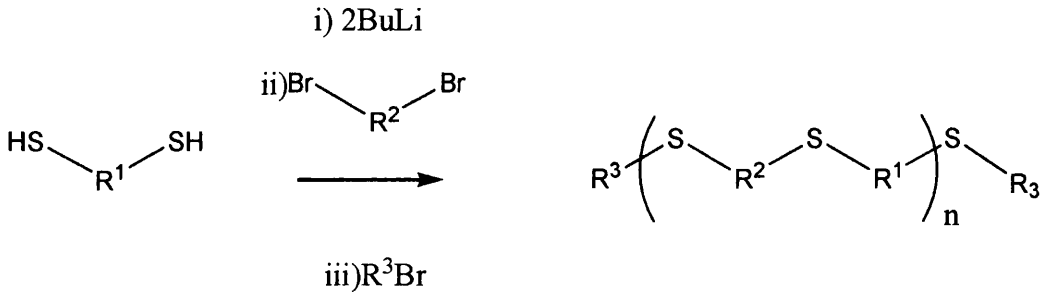
Chapter 2: Syntheses of branched polythiaalkanes from secondary dibromides and their use as catalysts for the chlorination of phenols.

2.1 Introduction to polythiaalkane synthesis.

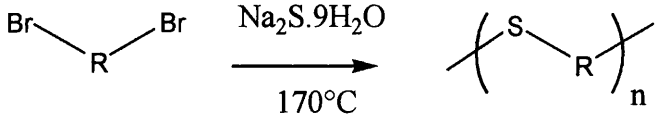
There are currently two polymer forming reactions that have been developed at the Centre for Clean Chemistry. The first Method[1] (Method A) involves the reaction of a dibromoalkane with a dithiolate (Scheme 2.1). A bromoalkane (often *n*-bromobutane) is added during propagation and reacts to form a terminal alkyl group (R^3). One mole equivalent of the dithiol reacts with 2 mole equivalents of butyllithium to form the dithiolate. Then 0.9 mole equivalents of the dibromoalkane is added prior to 0.2 mole equivalents of the bromoalkane (Scheme 2.1).



Scheme 2.1: Method A polymer forming process by the reaction of a dithiolate with a dibromoalkane.

This method is versatile in the fact that 'unsymmetrical' polymers can be synthesised containing different spacer groups. However, the lithiation procedure involves several steps, excessive cooling (-78°C) and the use of the moisture sensitive and expensive butyllithium which makes this method inappropriate for potential large scale synthesis.

The second method[2] (Method B) involves heating a dibromoalkane in the presence of sodium sulfide (Scheme 2.2).



Scheme 2.2: Method B polymer forming process by the reaction of sodium sulfide with a dibromoalkane.

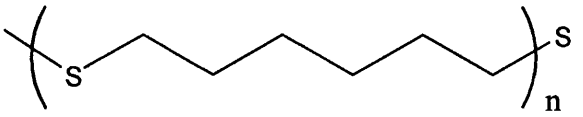
This method has several advantages over Method A, most notably in terms of cost and the simplicity of the reaction, which makes it much more applicable for large scale commercial synthesis. However, current methodologies allow only one type of spacer group to be incorporated into each individual polymer, making it less synthetically versatile than Method A.

2.2 An introductory note on the polymer nomenclature adopted in this thesis.

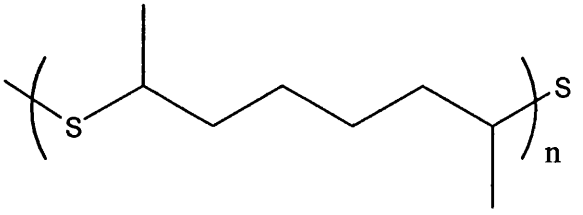
The IUPAC systematic names will be used in this thesis but will only appear in the experimental section. Preferentially the polymers will be allocated a number based on their sequential appearance in the text and will be referred to as **Polymer n**. Additionally linear polythiaalkanes will be classified with relation to the number of carbons in their spacing units. For example a polymer synthesised by Method A using 1,6-hexanedithiol and 1,8-dibromodecane will be referred to as Polymer 6-8. Polymers that contain only one main spacing unit, such as all polymers synthesised by Method B will be classified comparatively by the repetition of the number. *i.e.* a polymer synthesised from 1,6-dibromohexane by Method B will be referred to as Polymer 6-6. See also the *Reference Guide* located at the front of this thesis.

2.3 Establishment of the target polymer.

As stated in chapter 1 linear polythiaalkanes can be used as selective catalysts for the chlorination of phenols, but no branched polymers have been synthesised. As previously stated one method of increasing the selectivity of the chlorination system is to increase the steric factors associated with the chlorinating species or catalyst. It is for these reasons that it seemed desirable to synthesise a branched polythiaalkane. Due to the high selectivity achievable using the polythiaalkanes with 6 carbons in the repeating unit (**Polymer 1**; Figure 2.1), it seemed desirable to synthesise an analogous branched polymer (**Polymer 2**; Figure 2.1).



Polymer 1



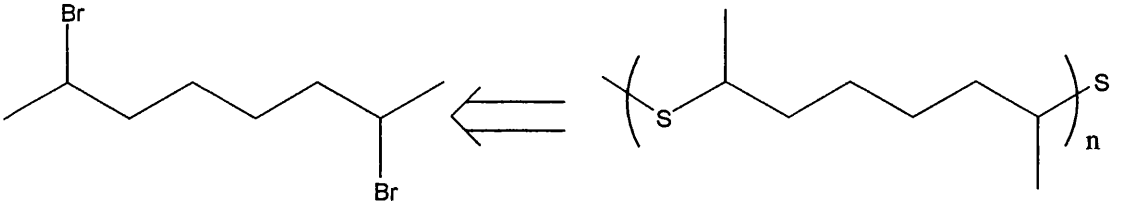
Polymer 2

Figure 2.1: The selective linear Polymer 6-6 (**Polymer 1**) and the target **Polymer 2**.

It seemed appropriate to introduce a small degree of steric hindrance in the vicinity of the sulfur atom and therefore **Polymer 2** was the initial target polymer.

2.3.1 A retrosynthetic approach to the synthesis of Polymer 2.

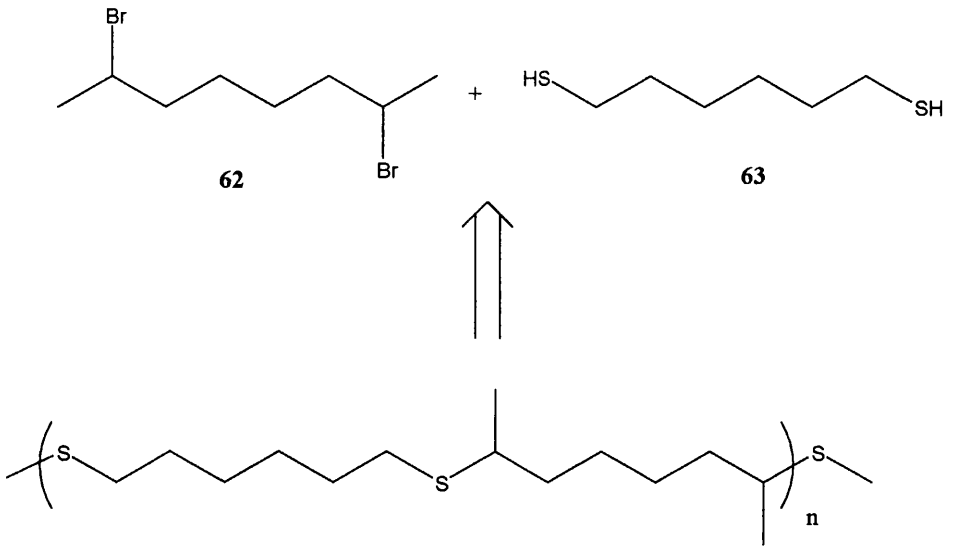
Using Method B it was initially assumed that a di-secondary bromide would react analogously to the di-primary bromides in these procedures, and therefore form a branched polymer. For example it originally seemed possible to synthesise **Polymer 2** from 2,7-dibromooctane (**62**, Scheme 2.3).



62 **Polymer 2**

Scheme 2.3: Retrosynthetic route to target **Polymer 2** *via* Method B.

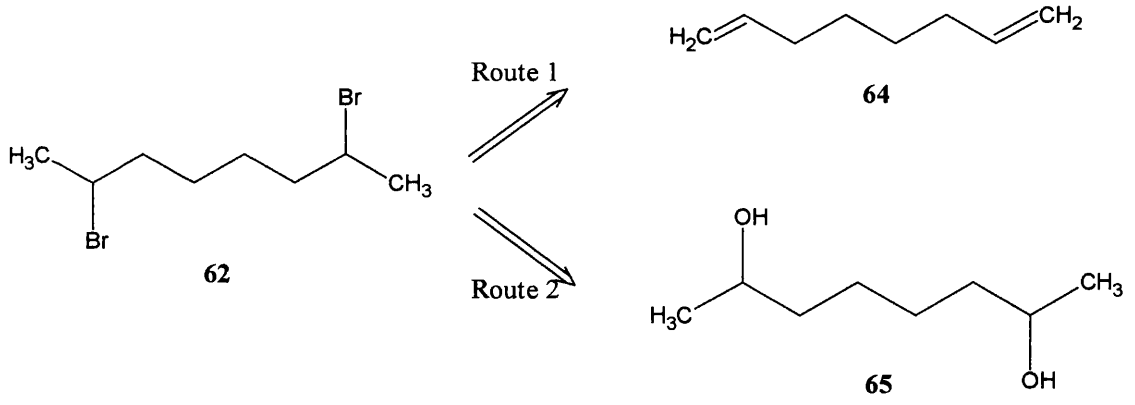
Analogously it seemed feasible that a *semi* branched polymer could be synthesised using Method A (Scheme 2.4).



Polymer 3

Scheme 2.4: Retrosynthetic route to semi branched **Polymer 3** *via* Method A from 2,7-dibromooctane (**62**) and 1,6-hexanedithiol (**63**) .

2,7-Dibromooctane (**62**) is not commercially available and therefore needed to be synthesised. The 2 main retrosynthetic strategies for achieving this are illustrated in Scheme 2.5.



Scheme 2.5: Retrosynthetic routes to 2,7-dibromooctane (**62**) from the 1,7-octadiene (**64**) and 2,7-octanediol (**65**).

Route 1 involves the Markownikoff addition of HBr across the double bond. The selectivity of this reaction would be difficult to control.[3] Even with careful control of conditions, such as to exclude light and peroxides and to use radical scavengers, the reaction is likely to produce significant amounts of the unwanted regioisomers 1,7- and 1,8-dibromooctane, which would be very difficult to remove.

Route 2 involves the substitution of a diol to produce the dibromooctane; depending on the bromination procedure used varying degrees of regioselectivity are achievable, and this route is potentially far more selective than route 1; therefore, a synthetic route *via* 2,7-octanediol (**65**) was chosen.

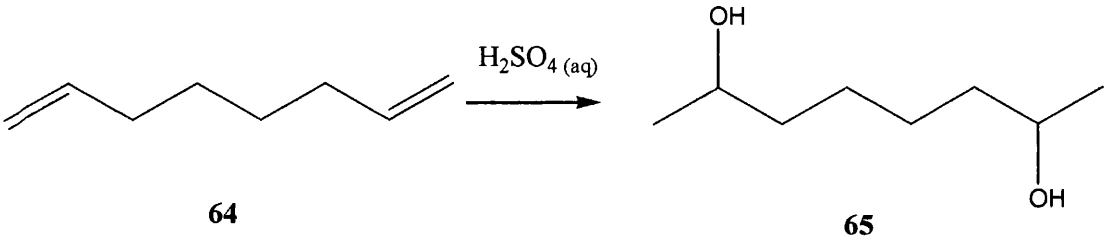
2.4 Synthesis of 2,7-octanediol.

2,7-Octanediol (**65**) itself is not commercially available and therefore requires synthesis. There are, of course, various potential routes to this diol, as alcohols can be synthesised by various methods. Common retrosynthetic strategies involve Grignard reactions, hydration of alkenes, or the reduction of carbonyl containing compounds.

The approaches involving the reduction steps can be instantly discarded due to the unavailability of any oxidised equivalents. The hydration step was therefore attempted in the first instance.

2.4.1 Acid catalysed hydration of 1,7-octadiene.

The hydration of alkenes can be facilitated using aqueous sulfuric acid (Scheme 2.6).



64 **65**

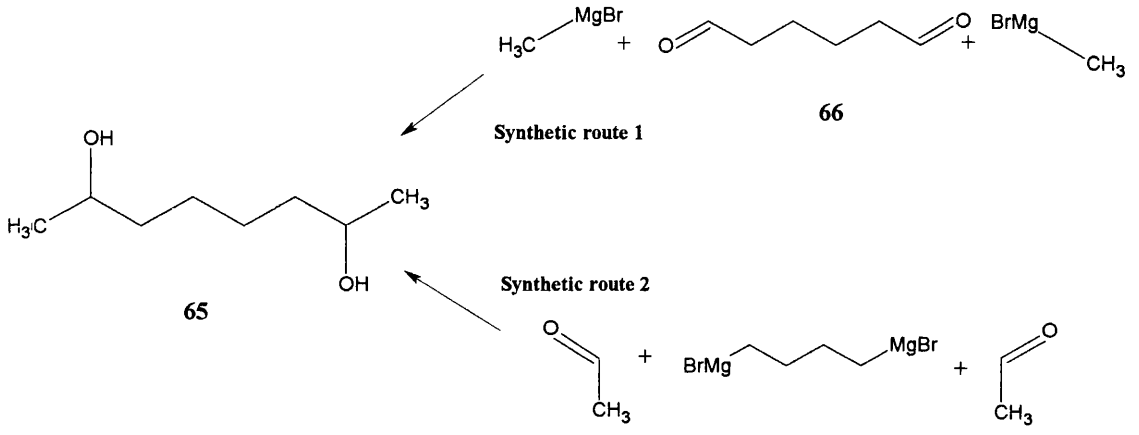
Scheme 2.6: Proposed synthetic route to 2,7-octanediol (**65**) by the hydration of 1,7-octadiene (**64**) facilitated by aqueous sulfuric acid.

The hydration procedure followed was adapted from a textbook reaction which hydrates 1-octene to 2-octanol.[4] However, although numerous attempts at this hydration were undertaken no desired product was isolated. A brown tar-like material was persistently formed, from which no identifiable organic compounds were isolated despite the application of various separation techniques. The tars obtained persistently gave rise to a broad signal between 0.5 and 2.5 ppm in the proton NMR spectrum. It is conceivable that

the alkene groups undergo cationic polymerisation where the initiation step is the simple formation of the cation by sulfuric acid and where the propagation involves nucleophilic attack of other alkene groups.

2.4.2 Grignard strategies.

Attention was next turned to potential Grignard reactions. Two potential synthetic routes of this type are illustrated in Scheme 2.7.

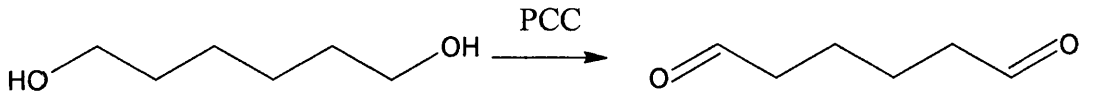


Scheme 2.7: Synthetic routes to 2,7-octanediol (**65**) *via* Grignard reactions.

Out of the two Grignards steps proposed, **Synthetic route 2** has been carried out previously but proceeded in low yield.[5] Therefore, it seemed desirable to investigate the alternative route. However, 1,6-hexanedial (**66**) is not commercially available and therefore required synthesis.

2.4.3 Oxidation of 1,6-hexanediol.

The oxidation of primary alcohols to aldehydes is commonly conducted with Cr(VI) reagents.[6] The oxidation facilitated by the widely utilised pyridinium chlorochromate (PCC)[7] was undertaken using the typical procedure[8] which was adapted for the diol (Scheme 2.8).



67 **66**

Scheme 2.8: Synthesis of 1,6-hexanedial (**66**) by PCC oxidation of 1,6-hexanediol (**67**).

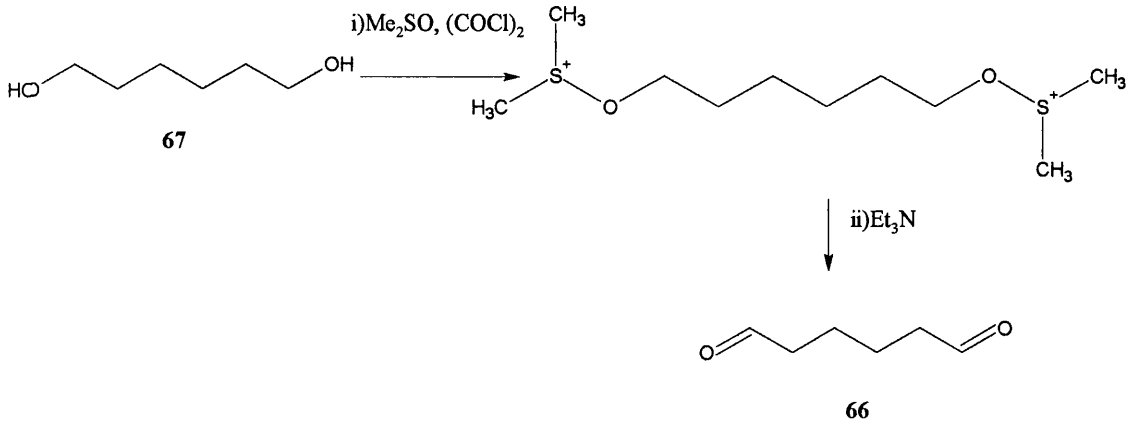
Following oxidation a relatively small amount of product was recovered. Furthermore, the major product was 6-hydroxyhexanal. 1,6-Hexanedial (**67**) was formed, but was not isolated as a pure material but only as a mixture with 6-hydroxyhexanal after reduced pressure distillation. Column chromatography was attempted to separate the mixture but no desired product was eluted from the column.

The typical PCC oxidation for a primary alcohol proceeds in high yield and during isolation the relatively large difference in boiling points between the alcohol and aldehyde is exploited in order to separate them by distillation. However, for this diol (**67**) the reaction appeared to be prevented from going to completion due to the excessive formation of a thick black gum. Also the large difference between the physical properties of the starting material and product could not be exploited due to the high abundance of the semi oxidised intermediate.

The low yields of organic material and the incompletion of the reaction may be explained by the observation that as the reaction proceeded the PCC is reduced and forms a relatively large amount of a thick insoluble black gum which can no longer be stirred efficiently even with a mechanical stirrer. Consequently, inefficient interaction between the reactants makes it difficult for the reaction to go to completion. The gum was formed in a relatively large volume as 3 mole equivalents are required to oxidise 1 mole equivalent of the diol. Washing of the black gum was time consuming and inefficient, as even after washing the black gum vigorously with organic solvents only a low yield of organic material was recovered.

The use of PCC on alumina was conducted using the literature method,[9] in an attempt to produce a less gummy precipitate that would be easier to wash. However, this did not appear to have a significant effect on the reaction; the stirring was once again difficult to maintain and ultimately a low yield of an impure crude product was once again obtained.

An alternative oxidation was next attempted. The Swern oxidation as illustrated in Scheme 2.9 seemed an obvious candidate with reported quantitative yields for many differently situated hydroxyl groups.[10]



Scheme 2.9: Synthesis of 1,6-hexanedial (**66**) by Swern oxidation of 1,6-hexanediol (**67**).

The Swern oxidation proceeded to a significant extent as observed by the detection of aldehyde protons (O=C-*H*) at around 10 ppm in the ^{1}HNMR spectrum of the crude product. However, it was also clear that a significant amount of alcohol groups remained due to the signal at around 3.5 ppm (the ratio of aldehyde proton : protons on hydroxyl carbon = 2.6:1). It was observed that 1,6-hexanediol (**67**) was partially insoluble in the oxidation medium, and this solvation problem was probably responsible for preventing the reaction proceeding quantitatively. The insolubility of the substrate is a known limitation to the Swern oxidation, and therefore excess dimethyl sulfoxide was then used to try to improve the solvation. The crude product of this reaction proved to be primarily the desired dial (**66**) in an 89 % yield. However, the crude product formed by the reaction was initially a colourless oil, but was converted into a rubber like brown/green gel upon standing. This is because the crude mixture is highly susceptible to polymer formation. 1,6-Hexandial has seldom been isolated, with the majority of reported preparations using it in tandem reactions or involving isolating it as a derivative because numerous researchers have highlighted its susceptibility to polymerisation.[11]

In an attempt to store the crude material the reaction was repeated and the crude product was stored as a dilute solution within a refrigerator, but upon removing the solvent, once again the gel like material was present. The polymer forming process is likely to be of the aldol type. The PCC oxidation product seemed less susceptible to polymer formation,

probably because it contained a significant amount of 6-hydroxyhexanal, but did form a rubber-gel material (polymer) when heat was applied during distillation. Like the above material described this crude product was not eluted from a silica column, despite the application of polar solvents such as methanol. It is possible that the compound was polymerising on the column, possibly by acid catalysed aldol reactions due to the acidic silica. However, this can not be verified as a neutral alumina column also resulted in no material being eluted even when large volumes of polar solvents (MeOH) were used for elution. The crude Swern product may be more susceptible to the aldol reaction due to the work up with triethylamine which may lead to base catalysed aldol reactions (Figure 2.2) after work-up.

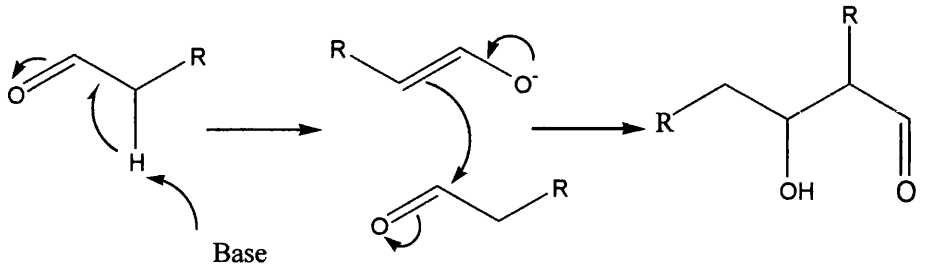
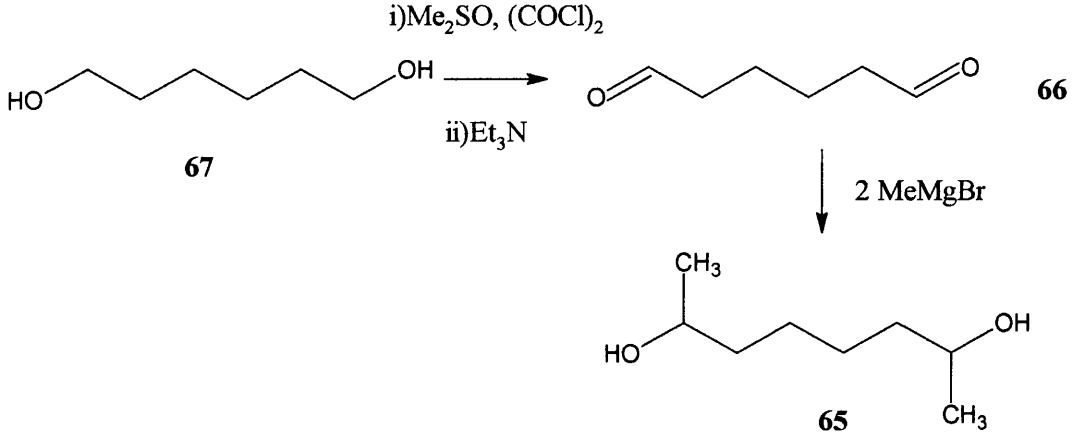


Figure 2.2: Base catalysed aldol reaction.

In an attempt to avoid such polymerisation the crude product was used directly in the next step without isolation. A typical Grignard[12] method was applied to the crude oxidation product (Scheme 2.10).



Scheme 2.10: Synthesis of 2,7-octanediol (**65**) by the formation of 1,6-hexanedial (**66**) by Swern oxidation of 1,6-hexanediol (**67**) followed by a Grignard reaction with MeMgBr.

The oxidation product was dissolved in dry THF and treated with 2 mole equivalents of methylmagnesium bromide. The crude product of the Grignard step was sent for NMR and MS analysis. It was clear that the desired 2,7-octanediol (**65**) had been synthesised due to the information obtained. Negative electrospray mass spectrometry detected anions at 145 m/z due to the $[M-H]^-$ ion, and at 129 due to the $[M-OH]^-$ ion. Some larger molecular weight material (300-600 m/z) was also present and was observed by positive electrospray mass spectrometry. The ^{1}HNMR and ^{13}CNMR spectra also showed the desired compound to be the major component but with signals from other species also being present, probably the larger molecular weight material detected by mass spectrometry. TLC analysis showed a complex mixture of at least 6 different components. The use of an impure dial (**66**) is probably partially responsible for this complicated mixture, but primarily the high susceptibility of the oxidation product to polymerisation (enhanced in basic media) is likely to be responsible for the impurities detected.

The ^{1}HNMR spectrum of the polymer gave rise to numerous signals between 1.0 and 5.5 ppm, a signal at around 6.8 ppm and an aldehyde peak at around 9.8 ppm. This complicated spectrum is the likely result of the formation of a range of different groups by the expected aldol addition and condensation reactions (Figure 2.3). The groups expected that are likely to be responsible for the numerous signals observed include aldehydes, aldols, α,ß-unsaturated aldehydes and alkene groups.

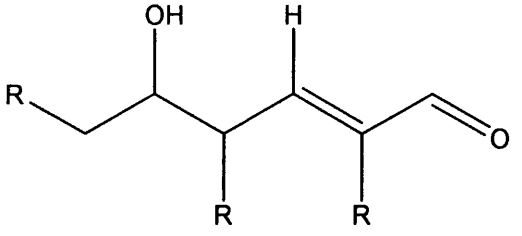
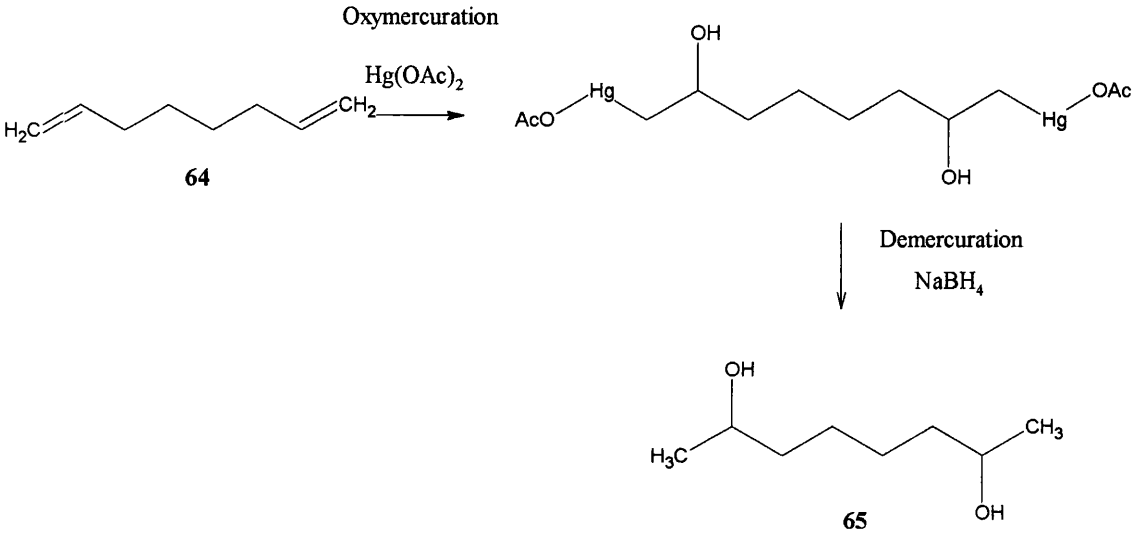


Figure 2.3: A typical arrangement of groups that may form during polymerisation by aldol addition and condensation.

An alternative route to the 2,7-octanediol (**65**) was chosen over any further attempt to purify the mixture because of the complex TLC and the low amount of recovered organic material (25 %) making it very unlikely that the desired compound could be isolated in high yield and purity by this synthetic route.

2.4.4 Oxymercuration-demercuration of 1,7-octadiene .

Following the failure of the Grignard route and the acid catalysed hydration of 1,7-octadiene (**64**) an alternative hydration step was then carried out. The oxymercuration demercuration[13] procedure is a well established method of hydrating alkenes and the typical procedure was adapted[14] to the diene (Scheme 2.11).



Scheme 2.11: Synthesis of 2,7-octanediol (**65**) by oxymercuration-demercuration hydration of 1,7-octadiene (**64**) facilitated by mercury (II) acetate.

The reaction was initially conducted using 25 mmol of the 1,7-octadiene (**64**) which was added to 50 mmol of the mercury (II) acetate. The sodium borohydride was added as a solution in sodium hydroxide at such a rate that the reaction temperature did not rise above 25 °C. After simple aqueous work up the crude material was subjected to reduced pressure distillation and two components were isolated which corresponded to 11 % of oct-7-en-2-ol and 47 % of the desired 2,7-octanediol (**65**). NMR and GC analysis of the diol indicate that it was isolated cleanly with no other regioisomers formed.

In order to produce a sufficient amount of diol (**65**) the oxymercuration procedure was repeated numerous times. The reaction was conducted twice using 100 mmol of 1,7-octadiene (**64**) and curiously resulted in a significant lower yield of only 12 % of diol (**65**) being isolated on both occasions. The reaction was then repeated three times using 50 mmol of diene. The isolated yields of these reactions were inconsistent with yields of 36, 25 and 50 % obtained. The results are shown in Table 2.1.

Table 2.1: Results for the $Hg(OAc)_2$ facilitated hydration of 1,7-octadiene (**64**).[a]

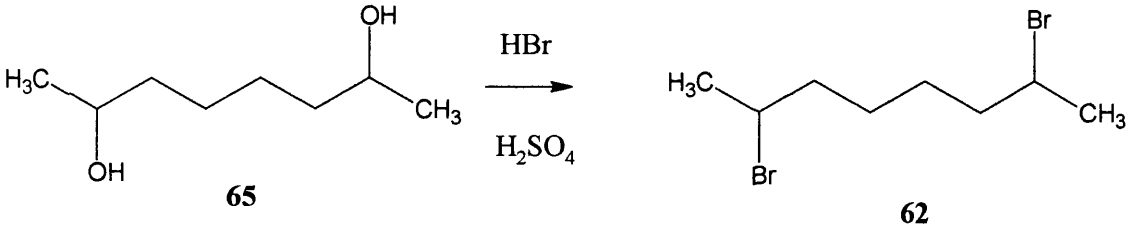
Reaction scale/mmol of 1,7-octadiene	Isolated yield of 2,7-octanediol/ mol %
25	47
100	12
100	12
50	36
50	25
50	50

[a] 1,7-Octadiene was reacted with 2 mole equivalents of mercury (II) acetate followed by reduction with excess $NaBH_4$. For more details see Section 2.18.5.

2.5 Synthesis of 2,7 dibromooctane

The substitution of a hydroxyl group by bromide can be conducted with a wide range of reagents, which are briefly discussed in this section. A common reagent for the substitution is HBr, which is normally employed as a 48 % aqueous solution.[15] The hydrobromic acid substitution of primary alcohols proceeds *via* an S_N2 mechanism in good yield. Secondary and tertiary alcohols prefer a S_N1 mechanism, which often results in a certain degree of rearrangement of the carbocation intermediate to give a mixture of regioisomers.[16] However, despite the potentially poor regioselectivity the HBr substitution was carried out on 2,7-octanediol (**65**) initially in the presence of sulfuric acid[17] (Scheme 2.12).

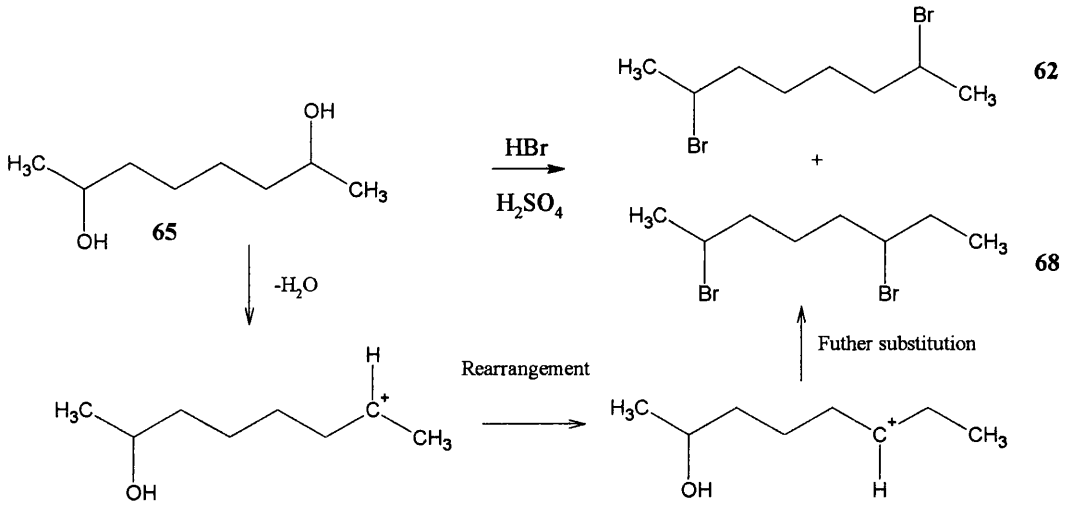
2.5.1 Hydrobromination of 2,7-octanediol



65 **62**

Scheme 2.12: Synthesis of 2,7-dibromooctane (**62**) by HBr substitution of 2,7-octanediol (**65**).

As predicted the reaction proceeded in an unselective manner to give a significant amount of the unwanted 2,6-dibromooctane (**68**), presumably as a result of side chain reactions such as those illustrated in Scheme 2.13.



Scheme 2.13: Synthesis of 2,7-dibromooctane (**62**) by HBr substitution of 2,7-octanediol (**65**), together with formation of 2,6-dibromooctane (**68**) by rearrangement of the carbocation intermediate.

A ratio of 2,7-:2,6-dibromooctane of around 3:1 was observed by GC and NMR analysis.

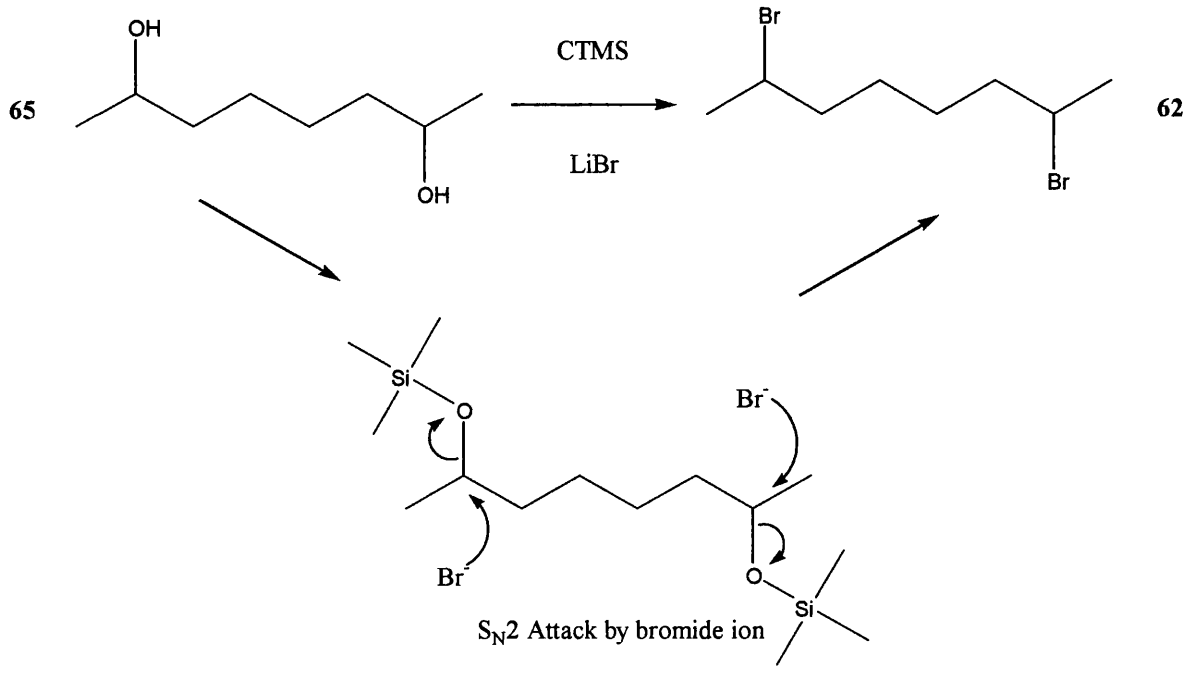
2.5.2 Hydrobromination of 2,7-octanediol in the absence of sulfuric acid

The reaction was also carried out in the absence of the concentrated sulfuric acid, and this time there was significantly more rearrangement with the isolated dibromides having a ratio of 2,6:2,7 of 1.9:1 as determined by ^{1}HNMR and 1.4:1 as determined by GC analysis. In this case, the GC method is probably the less accurate because there is overlap between the corresponding peaks, which probably results in an inaccurate integration.

2.5.3 S_N2 Substitution of 2,7-octanediol by CTMS and LiBr.

In order to avoid the rearrangement of the carbocations the general strategy is to ensure the reaction proceeds *via* an S_N2 mechanism. This is normally achieved by sulfur or phosphorus based reagents. Two of the most commonly used reagents are PBr_3[18] and

$SOBr_2$.[19] However even though these reagents are more regioselective than HBr they do not exclude rearrangements completely, which could still give rise to a mixture of regioisomers for the substitution of this diol. A more regioselective method involves the use of chlorotrimethylsilane (CTMS) in the presence of LiBr.[20] This reaction proceeds without rearrangement *via* the silyl ether, and this method was therefore applied to the 2,7-octanediol (**66**, Scheme 2.14).



Scheme 2.14: Synthesis of 2,7-dibromooctane (**62**) by S_N2 reaction of 2,7-octanediol (**65**) with CTMS and LiBr *via* the silyl ether.

Analysis of the crude reaction product indicated the formation of the desired 2,7-dibromooctane (**62**) but also indicated that there was a significant amount of a by-product formed. The by-product failed to separate from the desired dibromoalkane by column chromatography or reduced pressure fractional distillation. The ^{1}HNMR initially indicated that this by-product may have been 2-bromo-7-chlorooctane (**70**, Figure 2.5) due to a multiplet at 3.9 ppm and a doublet at 1.5 ppm, which strongly suggested a secondary chloride. GC also agreed with this possibility as the by-product had a shorter retention time, consistent with the more volatile chloride.

GCMS was used to confirm that the by-product was actually the 2-bromo-7-chlorooctane (**70**). A ratio of 2,7-dibrooctane to 2-bromo-7-chlorooctane of 3.3:1 by GC was obtained. The electrospray GCMS did not give any molecular ion peaks for these two species because bromine is a very good leaving group and is generally lost to

form the detectable cation or eliminated to form an alkene. The 2,7-dibromooctane fraction gave peaks at 191 and 193 m/z probably due to the formation of ion **69** as a result of the loss of a bromine atom from the molecular ion (Figure 2.4).

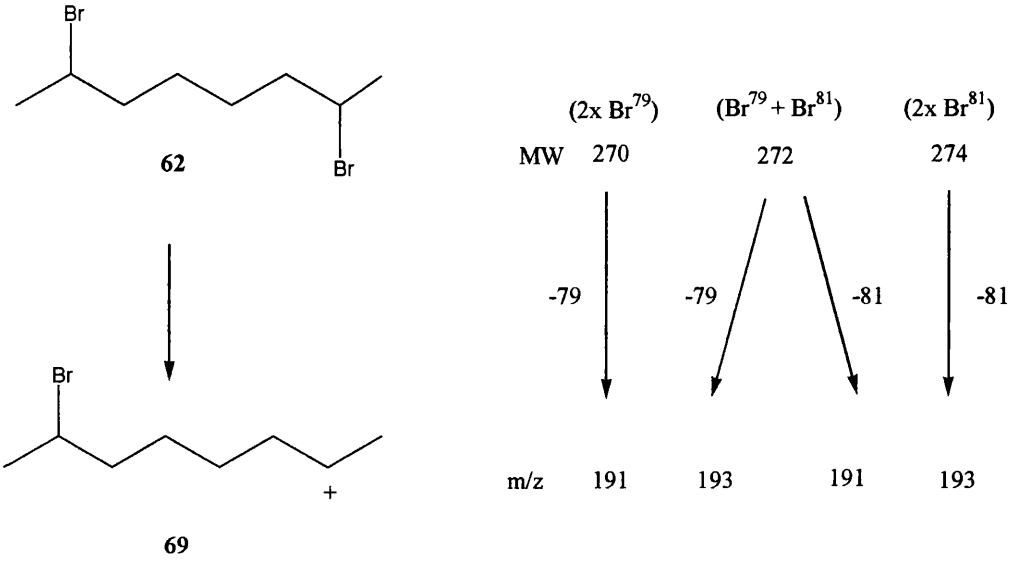


Figure 2.4: MS fragmentation of 2,7-dibromooctane (**62**) to give the detected ion **69**.

The 2-bromo-7-chlorooctane (**70**) peak fragmentation pattern is simpler than might have been expected because a bromine atom, which is a better leaving group than a chlorine atom, is selectively lost (Figure 2.5). No fragment ions were detected for the initial loss of a chlorine atom.

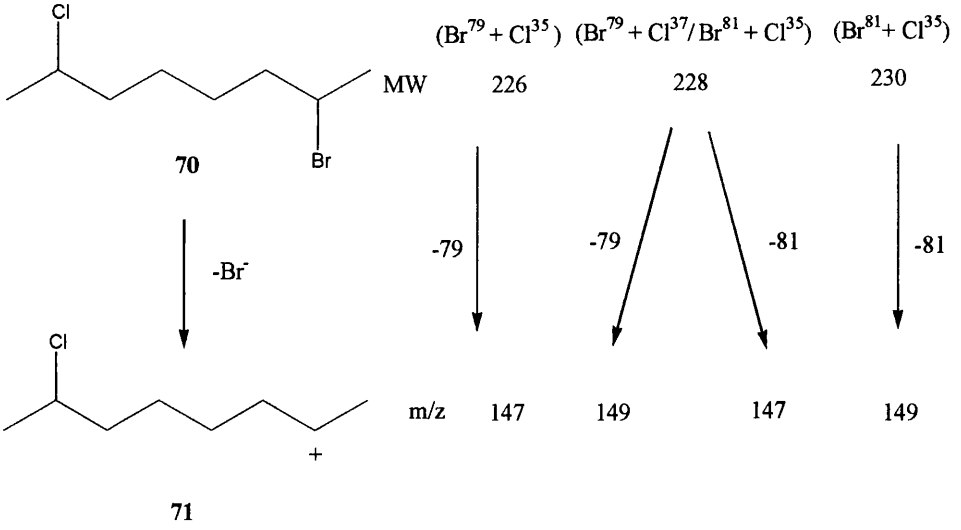
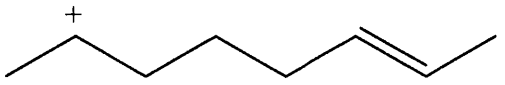


Figure 2.5: MS fragmentation of 2-bromo-7-chlorooctane (**70**) to give detected ion **71**.

In both GCMS peaks the most abundant fragment (100 %) appeared at 111 m/z and is presumably formed by the elimination of one molecule of hydrogen halide to from an alkene and the loss of one halogen atom form the molecular ion **72**. A structure of a possible ion is shown in Figure 2.6.



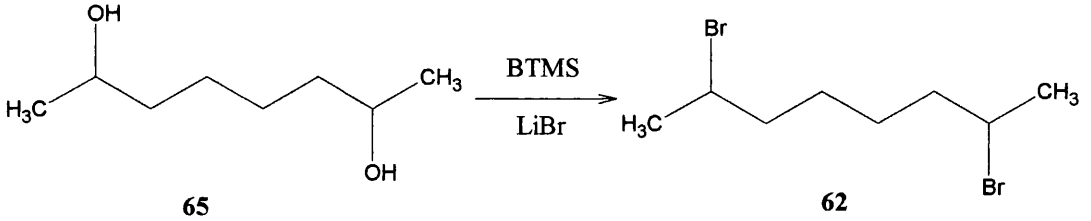
72

Figure 2.6: MS fragment ion (**72**), m/z = 111

The formation of the 2-bromo-7-chlorooctane is not completely unexpected as when the silyl ether is formed then a chloride anion is also generated and is able to act as the nucleophile in the S_N2 step. However, the primary literature does not seem to have any report of any similar findings.

2.5.4 S_N2 Substitution of 2,7-dibromooctane by BTMS and LiBr

To overcome the problem of chloroalkane formation the obvious solution was either to use more LiBr to increase the chance of the bromide ion being the successful nucleophile or simply remove the source of the chloride anion by using bromotrimethylsilane instead of the chlorotrimethylsilane (Scheme 2.15). The latter was the preferred option as it ensured that none of the chloroalkane can be generated, because even small amounts of the by-product would be difficult to remove.



65 **62**

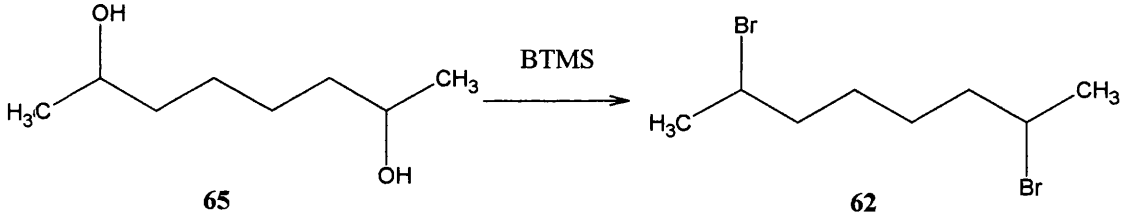
Scheme 2.15: Synthesis of 2,7-dibromooctane (**62**) by the reaction of 2,7-octanediol (**65**)and BTMS in the presence of LiBr.

Chlorotrimethylsilane was substituted for bromotrimethylsilane. The reaction was followed by TLC and took 42 h before the starting material was completely consumed, which is approximately twice as long as for the chlorotrimethylsilane reaction, presumably

because the formation of the silyl ether is slower with BTMS due to the bulkiness of the bromine atom.[21] All other experimental conditions remained the same. Surprisingly, in this case rearrangement occurred and there was a significant formation of the unwanted 2,6-dibromooctane (**68**). A 5.1:1 ratio for 2,7-dibromooctane to 2,6-dibromooctane was observed by GC analysis. This extent of rearrangement was not observed when the chlorotrimethylsilane was used. A possible explanation for this is that because the generation of the silyl ether is slower in this reaction and therefore there may be more time for the competing S_N1 reactions. The lithium bromide may generate a polar ionic environment that is effective in stabilising and encouraging the formation of cations, hence the observed rearrangement. The rearrangement is not seen to this extent by the use of BTMS without LiBr[22] which reinforces the hypothesis that the LiBr presence leads to the unexpected absence of regioselectivity.

The obvious solution was to attempt the substitution in the absence of LiBr (Scheme 2.16) which was next conducted.

2.5.5 S_N2 substitution of 2,7-dibromooctane by BTMS in the absence of LiBr catalyst.



65 **62**

Scheme 2.16: Synthesis of 2,7-dibromooctane (**62**) by the reaction of 2,7-octanediol (**65**) and BTMS.

This reaction was also followed by TLC analysis and once again the reaction proceeded slower, with the complete consumption of the starting material indicated after 92 h. The product was isolated by column chromatography in a yield of 89 %. GC and NMR analysis of the column product showed that it was a mixture of 2,6- and 2,7-dibromooctane in a ratio of 13:1. In order to obtain enough material to investigate the polymer forming steps and to synthesise a sufficient amount of the polymer for the testing as catalysts for the chlorination of phenols the reaction was repeated several times and the results are shown in Table 2.2.

Table 2.2: The results of BTMS substitution of 2,7-dibromooctane (**62**) in the absence of LiBr.[a]

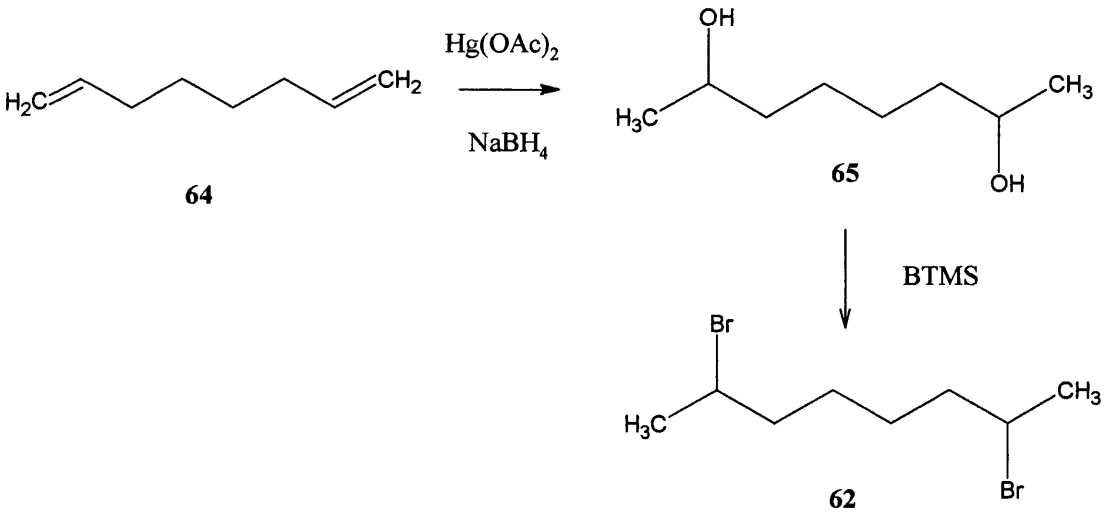
Temperature/ °C	Time/h	Isolated yield of dibromooctane/ mol %	2,7-dibromooctane:2,6-dibromooctane.[b]
50	92	89	13:1
50	92	83	46:1
50	92	77	11:1
50	92	89	38:1

[a] Reaction of 2,7-octanediol (10.3 mmol) with BTMS (41.1 mmol) in dry chloroform.

[b] As determined by GC peak area ratios.

The regioselectivity of the reaction was inconsistent, which was unexpected as the reaction conditions were apparently identical in each case. However, it was apparent from IR and NMR analysis of the isolated hydration product (2,7-octanediol, **65**) that sometimes small amounts of alkene groups were present, due to oct-7-en-2-ol impurities. From the IR spectrum of the staring material it was apparent that the lower regioselectivity was obtained when there were traces of alkene groups present. Therefore, it was originally speculated that the BTMS may react with the alkene groups present in oct-7-en-2-ol in a non regioselective fashion, or to liberate HBr which then reacts *via* a carbocation possibly to generate some 2,6-dibromooctane (**68**) and hence reduce the observed regioselectivity. This speculation was briefly investigated by the reaction of 1-octene with BTMS under the same conditions used above. After 92 h the product was worked up and the crude product was sent for NMR. The ^{1}HNMR integration indicated that 79 % of the 1-octene remained unreacted. There was 18 % of 2-bromooctane and 3 % 1-bromooctane accountable. No 3-bromooctane was formed. So it was clear that the low regioselectivity was not generated from the trace impurities of the alkene groups. No further investigation into the factors affecting the regioselectivity of this reaction was conducted and therefore no cause has been identified. Only the higher purity products (with ratios of 2,7-dibromooctane to 2,6-dibromooctane of 46:1 and 38:1) were used in the polymer forming steps.

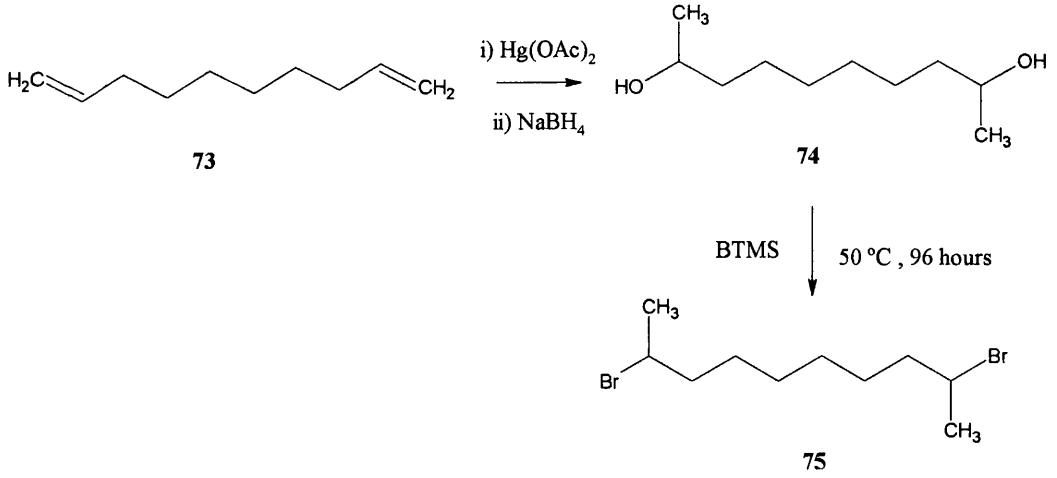
2.5.6 Derived synthetic route to 2,7-dibromooctane (Scheme 2.17).



Scheme 2.17: The derived synthetic route to 2,7-dibromooctane (**62**) by the mercury(II)acetate assisted hydration of 1,7-octadiene (**64**) and then S_N2 substitution of 2,7-octanediol (**65**) facilitated by BTMS.

Overall this synthesis represents a regioselective route to di-secondary bromides from the equivalent diene, the versatility of this route was briefly investigated by the formation of 2,9-dibromodecane (**75**) from 1,9-decadiene (**73**, Scheme 2.18).

2.6 Synthesis of 2,9-dibromodecane



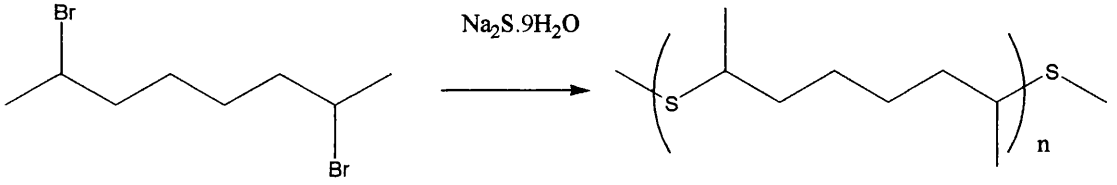
Scheme 2.18: Synthesis of 2,9-dibromodecane (**75**) by mercury(II)acetate assisted hydration of 1,9-decadiene (**73**) and substitution of 2,9-decanediol (**74**) by BTMS.

The hydration step proceeded to give a low yield of 15 % of the 2,9-decanediol (**74**), which was isolated by reduced pressure distillation. The bromination

step gave a 95 % yield of the dibromodecane (**75**) with a ratio of 2,9-dibromodecane:2,8-dibromodecane of 16:1 observed by GC analysis.

2.7 Attempted synthesis of Polymer 2 from 2,7-dibromooctane.

Polymer forming Method B was applied to 2,7-dibromooctane (**62**, Scheme 2.19). No mechanistic information was known about this substitution, and therefore it was unknown whether or not this procedure would be successful for secondary bromides.



62 **Polymer 2**

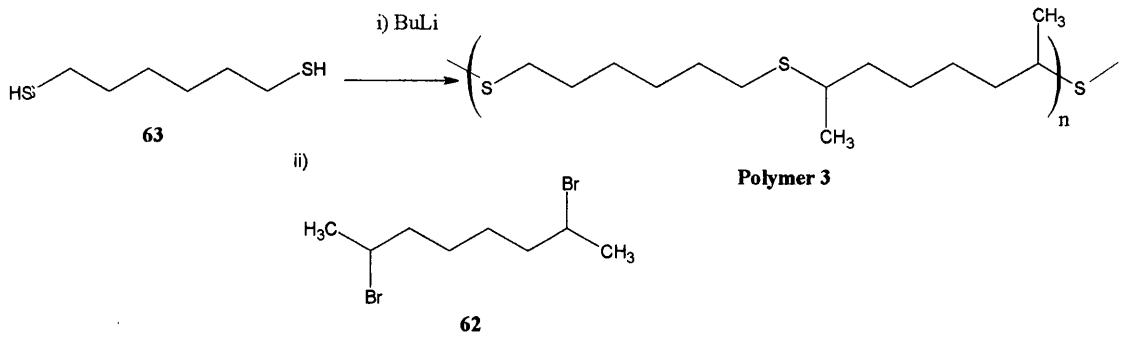
Scheme 2.19: Synthesis of **Polymer 2** by Method B reaction of 2,7-dibromooctane (**62**).

The reaction was carried out under the exact conditions that have proved successful for various di-primary bromides,[2] such as 1,6-dibromohexane. After work up only the starting material **62** was recovered (76 % recovery).

The fact that the reaction proceeded with primary bromides but not with secondary bromides indicates that the mechanism of the successful substitution may proceed *via* an S_N2 mechanism and therefore the secondary dibromide, which is relatively hindered, is more restricted and does not react. This type of steric effect is a widely appreciated restriction of the S_N2 mechanism.[23]

2.7.1 Attempted synthesis of Polymer 3

The alternative Method A procedure was followed (Scheme 2.20). This polymer step has also never been conducted on a secondary dibromide.



Scheme 2.20: Synthesis of semi branched **Polymer 3** by Method A reaction of 1,6-hexanedithiol (**63**) and 2,7-dibromooctane (**62**).

The reaction was carried out in an identical fashion to that which was successful with primary dibromides. During the reaction a thick white precipitate formed shortly after the addition of the butyllithium, and therefore, we can assume that the dithiolate formation was successful. During work up no insoluble polymer was formed unlike previous polymer formation reactions undertaken by this method. The organic phase was analysed by thin layer chromatography which showed two spots which correlated to 1,6-hexanedithiol (**63**) and 2,7-dibromooctane (**62**). The products were not worked up or analysed any further, partially due to the conclusive TLC result, but also because the 1,6-hexanedithiol is very odorous and is unpleasant to work with even when contained within a fume hood.

The reaction was carried out again and the 2,7-dibromooctane and the dithiolate were heated under reflux for 98 h as opposed to the previous reaction which was left to stir for 24 h. The TLC analysis indicated the same result. The 2,7-dibromooctane starting material was still present and the 1,6-hexanedithiol had been regenerated during work up.

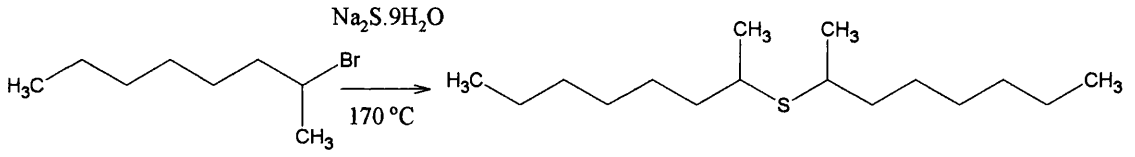
In summary, both the polymer forming reactions, Method A and Method B, had failed and the obvious conclusion was that the secondary dibromides are less susceptible to substitutions with the sodium and lithium thiolate nucleophiles than their primary bromide analogues.

2.8 Model investigation of the reactivity of 2-bromooctane with sodium sulfide.

To investigate this reactivity further a series of reactions were carried out using 2-bromooctane (**76**, Scheme 2.21) in the presence of sodium sulfide.

2.8.1 Reaction of 2-bromooctane with sodium sulfide under conditions analogous to the polymer forming Method B.

The initial reaction undertaken mimicked the conditions used in the attempted polymer formation, and therefore it was expected that no reaction would occur. The reaction was conducted using 1 mole equivalent of 2-bromooctane (**76**) and 0.5 mole equivalent of sodium sulfide nonahydrate (Scheme 2.21).



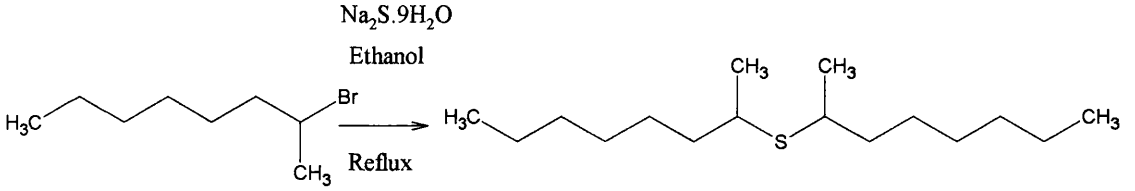
76 **77**

Scheme 2.21: Proposed synthesis of bis-(1-methylheptyl) sulfide (**77**) by reaction of 2-bromooctane (**76**) and sodium sulfide under conditions analogous to the polymer forming Method B.

After simple aqueous work up GC and NMR were used to confirm that the reaction did not proceed and that 97 % of the starting material (**76**) was recovered. The reaction was repeated with anhydrous sodium sulfide and essentially the same result was observed; 98 % of the starting material was recovered.

2.8.2 Reaction of 2-bromooctane with sodium sulfide under reflux in ethanol.

From the literature it was observed that secondary bromides have previously reacted with sodium sulfide[24] to give the equivalent branched dialkyl sulfides. The method used in each case was a reflux in ethanol. The conditions used in the literature were adapted to the model (Scheme 2.22).



76 **77**

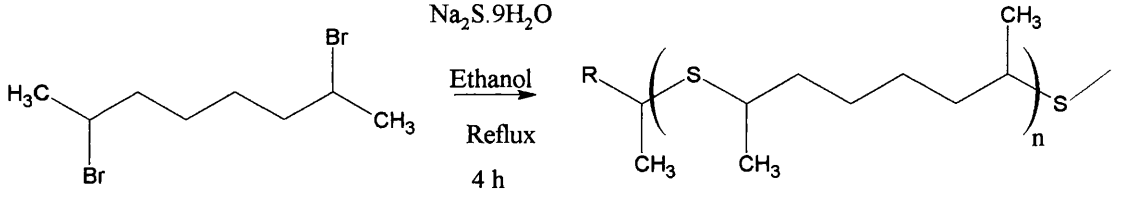
Scheme 2.22: Synthesis of bis-(1-methylheptyl)sulfide (**77**) by reaction of 2-bromooctane (**76**) and sodium sulfide under ethanolic reflux.

In this case the reaction proceeded successfully to give an isolated yield of bis-(1-methylheptyl) sulfide (**77**) of 87 % after multiple reduced pressure distillations. A racemic mixture of 2-bromooctane (**76**) was used and therefore the combinations of chiral centres possible in the product were R+R, S+S, R+S and S+R. The first two are a pair of enantiomers and the second two are the same meso compound and each set of pairs are diastereoisomers of each other. The diastereoisomers formed have different physical properties and were distinguishable. The GC trace of the compound gave an approximate 50/50 mixture of the two diasterioisomers.

The fact that the reaction proceeded in an ethanolic solution but not under solvent free conditions may indicate that the successful substitution proceeds *via* an S_N1 mechanism which is opened by the protic influence of the ethanol.

2.9 Synthesis of Polymer 2 by Method B under refluxing ethanol.

These model conditions were then adapted to the polymer forming reaction (Scheme 2.23)



62 **Polymer 2**

Scheme 2.23: Synthesis of **Polymer 2** form 2,7-dibromooctane (**62**) by a modified Method B procedure; reflux in ethanol.

After work up, the crude product was analysed by NMR. The NMR suggested that the desired substitution proceeded and very little of the bromide groups remained. However, the NMR also showed signals indicating alkene groups. The ^{1}HNMR integrals of the protons adjacent to sulfur (methine) and the alkene protons were compared and a CHS methine proton to alkene protons ratio of 2.1:1 was apparent.

From literature comparison the elimination pattern of this secondary bromide is that of expected[25] (Figure 2.6).

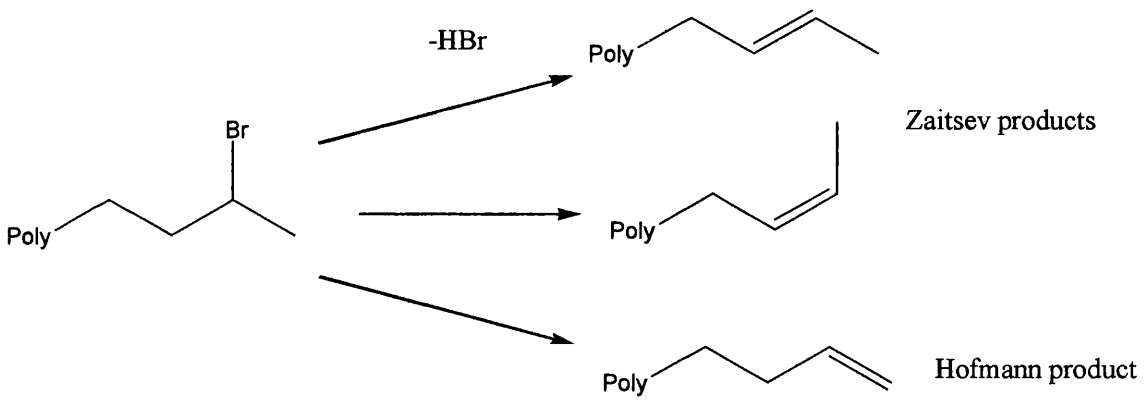
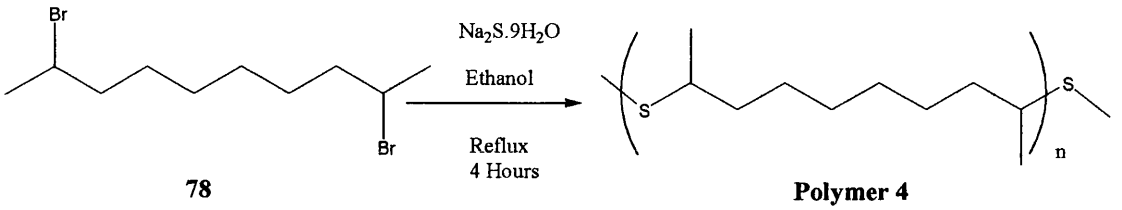


Figure 2.6: The competing elimination pattern observed during the polymer forming step.

The *trans*-Zaitsev product is the main elimination product. The *cis*-Zaitsev product and the Hofmann product are also accountable by proton and carbon NMR. The proton NMR gives the expected multiplet at 2.70 ppm which is due to the methine proton adjacent to sulfur (S-CH), and the expected doublet at 1.55 ppm which is due to the branched methyl groups. Within the polymer repeating unit all the protons except the lone methine proton adjacent to sulfur resonate between 1.00-1.60 ppm. The observed ratio between the methine proton to the rest of the protons was observed as 8.8:1. The predicted amount for the theoretical repeating unit for the polymer is 7:1. As elimination is occurring then it is expected that this ratio would in fact rise due to there being fewer methine protons relative to protons in the region of 1.00-1.60 ppm because of the formation of alkenes which generates in addition to alkenic signals at around 4.5 ppm some signals in the region of 1.00-1.60 due to protons on nearby carbons.

2.10 Synthesis of Polymer 4 by Method B under refluxing ethanol.

The same polymer forming conditions that were applied to 2,7-dibromooctane (**62**) were applied to the 2,9-dibromodecane (**78**) to determine whether the same degree of competition between elimination and substitution would be observed (Scheme 2.24).



78 **Polymer 4**

Scheme 2.24: Synthesis of **Polymer 4** by the reaction of 2,9-dibromodecane (**78**) under a modified Method B procedure ; reflux in ethanol.

The same reactivity pattern was observed with 2,9-dibromodecane (**78**). However, this time a considerably higher CHS methine proton to alkene protons ratio of 4.0:1 was apparent. The same alkene groups were identified and the ratio of the methine proton to the other protons was 10.0 :1 which is higher than the expected 9:1 for the same reasons stated above. There was considerably less elimination when 2,9-dibromodecane was used. This is not understood and it was originally speculated that there may be an anomaly in the results and/or the results may not be reproducible.

Therefore, the polymer forming reactions of 2,7-dibromooctane and 2,9-dibromodecane with sodium sulfide in the presence of ethanol were both repeated to see if the degree of elimination was a reproducible occurrence. The ratio of the CHS methine proton to alkene protons the second time for 2,7-dibromooctane was 2.3:1 which is very similar to the original 2.1:1. The second ratio observed for 2,9-dibromodecane was 4.1:1 once again being very similar to the original 4.0:1. It was concluded that there were no anomalies in the experimentation and that the degree of elimination is reproducible for a fixed set of conditions. However it is not understood why 2,7-dibromooctane gives a greater amount of alkene products relative to 2,9-dibromodecane.

There is clearly competition between substitution (polymerisation) and elimination. In the model reaction (Scheme 2.22) when the bis-(1-methylheptyl) sulfide (**77**) was isolated none of the elimination products (octenes **80-82**) were accounted for, but would have been removed during work up and isolation of the sulfide (**77**).

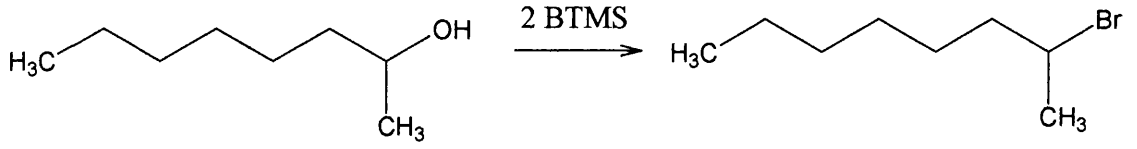
2.11 Further model investigations of the reactivity of 2-bromooctane with sodium sulfide.

Further investigations using the reaction of 2-bromooctane (**76**) with sodium sulfide were required to understand the relationship between elimination and substitution, and ultimately to promote the substitution and prevent the elimination.

2.11.1 Synthesis of 2-bromooctane

The 2-bromooctane (**76**) used in previous reactions was purchased from Lancaster Chemicals. The specification of the product was quite poor (see Table 2.4), and the sale of the chemical has since been discontinued. No other supplier seemed to supply the chemical. Similar 2-bromoalkanes such as 2-bromoheptane, 2-bromononane and 2-bromodecane, were also not available in high purity at a practical price.

The most desirable solution was to synthesise 2-bromooctane from commercially available 2-octanol (**79**). Due to previous experience in synthesising 2,7-dibromooctane, it was apparent that one of the most regioselective methods of producing secondary bromides from secondary alcohols is the substitution facilitated by bromotrimethylsilane (Scheme 2.25).



79 **76**

Scheme 2.25: Synthesis of 2-bromooctane (**76**) by BTMS substitution of 2-octanol (**79**).

The substitution with BTMS proceeds slowly. Therefore, the progress of the reaction was followed to determine when the reaction was complete. The reaction was initially followed by FTIR spectroscopy (Figure 2.7) to monitor the removal of the OH peak, and was later followed by the more quantitative method of GC (Table 2.3).

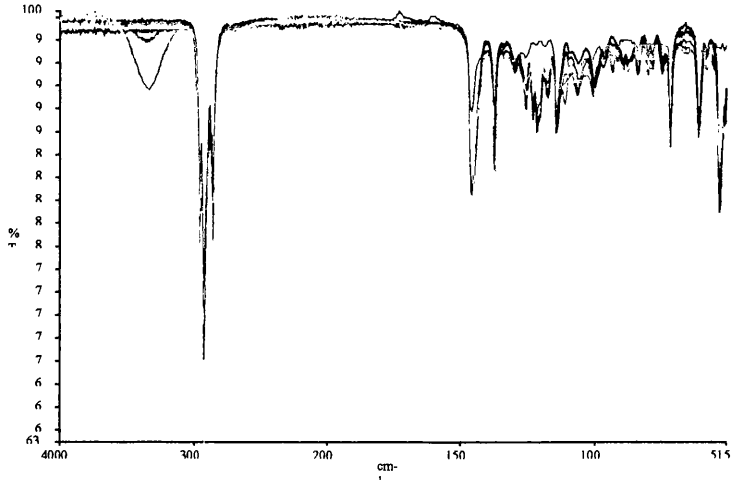


Figure 2.7: Infrared spectrum showing the progress of the reaction of 2-octanol (**79**) with BTMS.

Table 2.3: GC analysis of the substitution of 2-octanol (**79**) by BTMS.

Reaction time (h)	2-bromooctane (% area)[a]	3-bromooctane (% area)[a]	2-octanol (% area)[a]
72	75.1	2.3	22.7
96	82.4	3.5	14.1
120	86.8	2.4	9.2
144	92.2	3.0	4.8
168	92.5	2.8	4.8

[a] As obtained by GC, not relative to any internal standard.

It was apparent that the progress of the reaction appeared to stop after 144 h. After simple aqueous work-up followed by column chromatography 83 % of the 2-bromooctane (with about 3 % 3-bromooctane impurity) was isolated. The purity of this product was compared with that of the previously purchased 'Lancaster product' (Table 2.4).

Table 2.4: Comparison of the purity of the synthesised 2-bromooctane with the commercial 'Lancaster' product previously obtained.

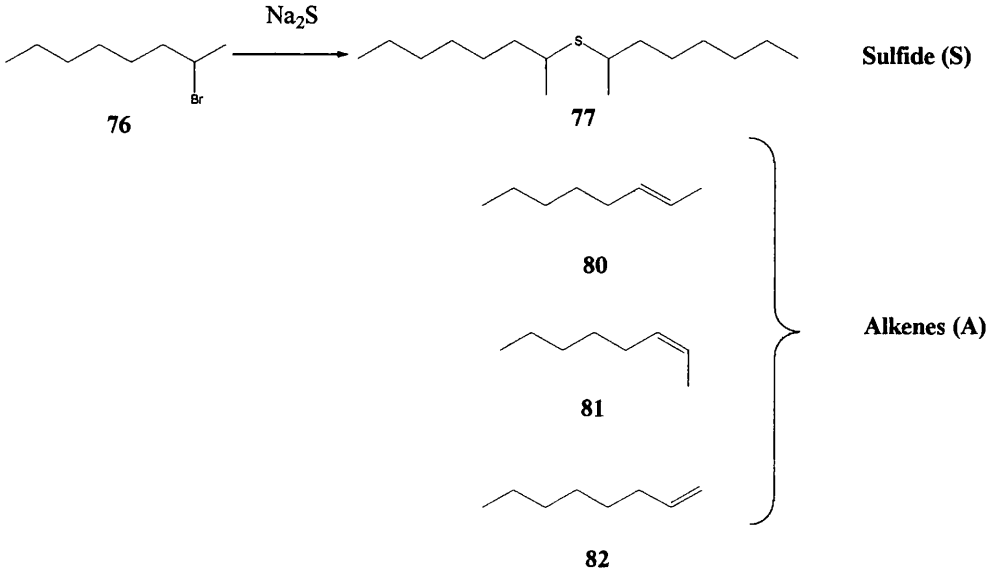
2-bromooctane	2-bromooctane (% area)	3-bromooctane (% area)	2-bromooctane: 3-bromooctane
Synthesised	97.3	2.7	36:1
Lancaster product	89.8	9.2	10:1

The product obtained was relatively pure, which was a requirement for the next investigation because the pattern of elimination and substitution may well have been complicated by the unwanted 3-bromooctane isomer.

2.11.2 Investigations of the reactivity of 2-bromooctane with sodium sulfide in various solvents.

In order to find out more about the factors that affect the reactivity of 2-bromooctane (**76**) with sodium sulfide, particularly the factors that control the competition between substitution and elimination, a series of reactions was initially

conducted in a range of different solvents. It was a requirement for the investigation to account quantitatively for the octenes generated. The expected products of the reaction were bis-(1-methylheptyl) sulfide (**77**), and a mixture of octenes (**80-82**, Scheme 2.26). The reactions were worked up by simple aqueous extractions. However, the organic phase was not evaporated due to the likelihood of losing the volatile octenes. Instead an internal standard (tetradecane) was added and the resulting mixture was analysed by GC (Table 2.5).



Scheme 2.26: The reaction of 2-bromooctane (**76**) with sodium sulfide in various solvents. The formation of bis-(1-methylheptyl) sulfide (**77**), *cis*- and *trans*- Zaitsev alkenes (**80**, **81**) and a Hofmann alkene (**82**).

Table 2.5: Results for the reaction of 2-bromooctane with sodium sulfide in various solvents[a]

Experiment code	Solvent	Time /h	Temp / °C	**76**/ mol %[b]	**77**/ mol %[b]	**80**/ mol %[b]	**82**/ mol %[b]	**81**/ mol %[b]	**S:A**	Mass balance
BRS1	EtOH	4	95	10.9	73.1	6.6	2.6	2.3	6.4	95.5
BRS2	DMSO	4	95	1.5	89.3	5.4	1.0	1.6	11.2	97.3
BRS3	DMF	4	95	10.9	77.2	7.2	0.8	1.3	8.3	97.4
BRS4	THF	6	80	90.3	0.0	0.0	0.0	0.0	-	90.3
BRS5	Acetone	6	65	84.5	7.2	0.0	0.0	0.0	-	91.7
BRS6	DMSO	14	60	0.8	88.3	5.6	1.0	1.4	11.0	97.1
BRS7	Dry DMSO	4	95	3.1	79.6	8.9	1.2	1.8	6.7	94.6

[a] 2-Bromooctane (5.18 mmol) was reacted with $Na_2S.9H_2O$ (2.85 mmol) in the stated solvent (5 mL) for the stated time at the stated temperature. See Scheme 2.26.

[b] Yields of 2-bromooctane (**76**), bis-(1-methylheptyl)sulfide (**77**), *cis* and *trans* 2-octene (**80**, **81**) and 1-octene (**82**) as determined by quantitative GC relative to tetradecane as an internal standard

The octenes (**80-82**) were identified by their response factors relative to pure samples and were double checked by the addition of the octenes to the product mixture to determine whether a new peak was formed, or an existing peak was enhanced.

The product octenes were identified as the two Zaitsev products (**80**, **81**) and the Hofmann product (**82**). These correlate exactly to the alkene groups observed in the polymeric sulfides previously synthesised (Figure 2.6). Despite the fact that 3-octyl groups are observed in the sulfide (Table 2.6), no 3-octene was visible in the GC trace. However, *trans*-3-octene was determined to have a similar response factor to 1-octene and therefore it is conceivable that small amounts of the 3-octene would be unrecognisable in the GC trace.

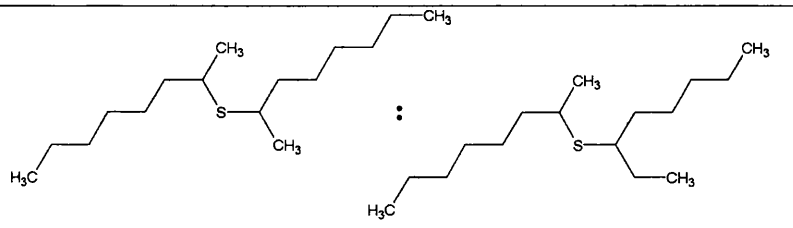
Table 2.5 shows that the substitution proceeds in very polar aprotic solvents such as DMF and DMSO and in protic solvents such as EtOH, but does not proceed well in less polar aprotic solvents such as acetone. Also, the reaction does not proceed at all in THF (aprotic, relatively low polarity). In each case where the reaction preceded the same pattern of elimination products was produced.

The highest sulfide to alkene ratios were observed in the presence of the polar aprotic solvents (DMSO and DMF).

As previously mentioned secondary bromides are susceptible to both S_N1 and S_N2 reactions and it is likely that under the reaction conditions both mechanisms would proceed. The S_N1 substitution is in direct competition with E1 elimination and therefore the greater the proportion of S_N1 relative to S_N2 then the more elimination would be expected. The first step in both E1 and S_N1 is identical and is the formation of the carbocation intermediate. The formation of the carbocation is promoted by polar protic solvents such as water or ethanol. To see whether the water present in the reactions was responsible for the observed elimination, the reaction was also carried out under dry conditions. Experiment BRS7 (Table 2.5) was carried out using anhydrous Na_2S and dry DMSO and proceeded in a similar manner to the non-dry reactions except for the unexpected drop in the sulfide to alkene ratio. However, the similar result suggests that a protic influence is not required to facilitate the reaction nor is it directly responsible for the observed elimination.

As previously stated the substitution proceeds to give 2-substituted and 3-substituted alkyl groups, as illustrated in Table 2.6.

Table 2.6: Ratio of bis-(1-methylheptyl) sulfide (**77, Sulfide 1**) to 1-methylheptyl 1-ethylhexyl sulfide (**Sulfide 2**) generated for the reaction of 2-bromooctane (**76**) with Na_2S.

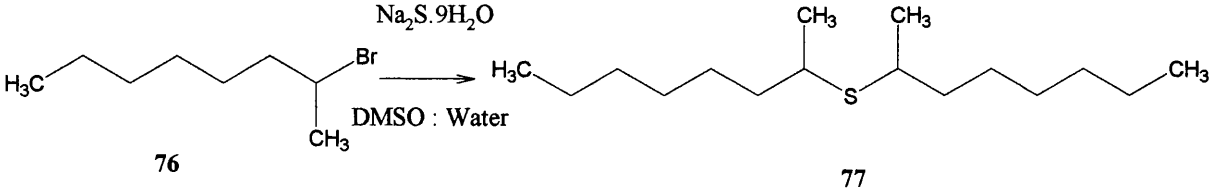
Experiment Code	 **Sulfide 1** : **Sulfide 2**
BRS1[a]	15.2:1
BRS2[a]	16.5:1
BRS3[a]	16.3:1
BRS6[a]	17.6:1
BRS7[a]	19.1:1

[a] See Table 2.5

In the starting material the ratio of 2-bromooctane to 3-bromooctane was determined as 36:1, if the reaction proceeded regioselectively (as in S_N2) then we would have expected the ratio of sulfide 1:sulfide 2 to be 17.5:1. In each case the ratio is close to the expected value (≈17.5 +/- 3). Considering the error of the GC instrumentation (up to 2-3 %) then it can assumed that there is little to no accountable rearrangement taking place.

2.11.3 Investigation of different DMSO:water solvent compositions on the reactivity of 2-bromooctane with sodium sulfide.

Curiously, as previously mentioned, when dry DMSO was used as the solvent it gave a significantly lower sulfide:alkene ratio. This observation prompted a further investigation into the effect that different water:DMSO solvent compositions may have on the competing substitution and elimination (Scheme 2.27). The results are shown in Table 2.7.



Scheme 2.27: The formation of bis-(1-methylheptyl)sulfide (**77**) by the reaction of 2-bromooctane (**76**) with sodium sulfide conducted using various DMSO:water solvent compositions.

Table 2.7: Influence of different DMSO:water solvent compositions.[a]

Experiment Code	Solvent DMSO%-Water%	**76**/ mol %[b]	**77**/ mol %[b]	**80**/ mol%[b]	**82**/ mol %[b]	**81**/ mol %	**S:A**	Mass balance
BRS7	100-0	3.1	79.6	8.9	1.2	1.8	6.7	94.6
BRS8	95-5	0.9	85.0	8.9	2.2	2.7	6.1	99.7
BRS10	75-25	1.8	83.1	9.0	2.3	2.9	5.9	99.1
BRS11	50-50	31.5	49.8	8.9	2.0	3.3	3.5	95.5
BRS9	25-75	82.0	8.8	5.5	1.3	2.3	1.0	99.9

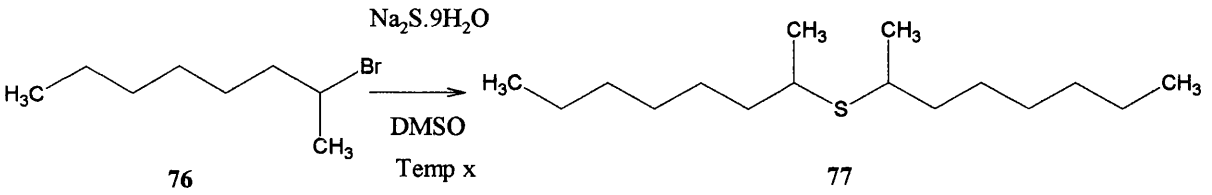
[a] 2-Bromooctane (5.18 mmol) was reacted with $Na_2S.9H_2O$ (2.85 mmol) in the stated solvent (made up to 5 mL)) at 95°C for 4 h. See Scheme 2.26.

[b] Yields of 2-bromooctane (**76**), bis-(1-methylheptyl)sulfide (**77**), *cis* and *trans* 2-octene (**80**, **81**) and 1-octene (**82**) as determined by quantitative GC relative to tetradecane as an internal standard

The results in Table 2.7 show that as the percentage water composition increases then there is a relative increase in the amount of elimination. This is likely to be due to the previously mentioned relationship between the protic nature of the solvent and the formation of carbocation intermediates. The extent of reaction decreases with increasing water composition. The reduction in the extent of the reaction is likely to be due to the increasingly limited solubility of 2-bromooctane (**76**), which is insoluble in water alone.

2.11.4 Investigation of the reactivity of 2-bromooctane with sodium sulfide under varying temperature.

At this stage of the investigation it was apparent that DMSO was the optimal solvent for promoting the substitution relative to elimination. This solvent was used in further investigations. The next variable investigated was temperature (Scheme 2.28). In general higher temperatures favour elimination[26] since the activation energy is higher in elimination reactions. The results obtained at different temperatures are reported in Table 2.8.



Scheme 2.28: The reaction of 2-bromooctane (**76**) with sodium sulfide at various temperatures.

Table 2.8: Results for the reaction of 2-bromooctane (**76**) with sodium sulfide at various temperatures.[a]

Experiment	Time / h	Temp / °C	**76** / mol %[b]	**77**/ mol %[b]	**80**/ mol%[b]	**82**/ mol %[b]	**81**/ mol %[b]	**S:A**	Mass balance
BRS2	4	95	1.5	89.3	5.4	1.0	1.6	11.2	97.3
BRS6	14	60	0.8	88.3	5.6	1.0	1.4	11.0	97.1
BRS 12b	24	50	18.2	71.1	4.5	1.2	1.2	10.2	96.2
BRS 13b	24	40	1.3	87.5	5.1	1.1	1.3	11.7	95.0
BRS 14	24	30	17.9	73.3	4.5	1.2	1.2	10.6	98.1
BRS 14b	72h	30	1.9	85.0	1.5	0.3	0.4	38.5	89.1
BRS 15	72h	RT	5.1	80.7	3.9	0.8	1.0	14.1	91.5

[a] 2-Bromooctane (5.18 mmol) was reacted with $Na_2S.9H_2O$ (2.85 mmol) in the DMSO (5 mL) at various temperatures for the stated duration. See Scheme 2.26.

[b] Yields of 2-bromooctane (**76**), bis-(1-methylheptyl)sulfide (**77**), *cis* and *trans* 2-octene (**80**, **81**) and 1-octene (**82**) as determined by quantitative GC relative to tetradecane as an internal standard.

As the results in Table 2.8 show, there was very little variation in the ratio of sulfide:alkene produced as the temperature was reduced form 90 °C to 30 °C. However, the last two entries to the table suggested an improved ratio, although the results are suspect due to the low mass balances. Experiments BRS14b and BRS15 were carried out using an open system (non sealed reflux condenser) over a period of 72 h. Experiments BRS14 and BRS14b were carried out under identical conditions and the difference between the two reactions was just their duration. After 24 h (BRS14) 73.3 % of the dialkyl sulfide (**77**) and 6.9 % of alkenes were formed with 17.9 % remaining 2-bromooctane (**76**). However, when the same conditions were maintained for 72 h (BRS14b) then as expected the reaction proceeded further, consuming more 2-bromooctane to leave only 1.9 % unreacted and giving 85.0 % sulfide. As more 2-bromooctane was consumed it would be expected that more dialkyl sulfide and more octenes would also be formed. However, only 2.2 % of octenes were detected. It is likely that over the period of 72 h some of the volatile octenes had been lost *via* evaporation from the open system. This would also account for the low mass balances of 89.1 % for BRS14b and 91.5 % for BRS15. Therefore, the amount of

alkene was probably underestimated. With the exception of the misleading experiments BRS15 and BRS14b there was no significant increase in the sulfide to alkene ratio, and it can be concluded that a reduction in temperature has no significant effect on the competition of elimination and substitution in this reaction.

2.11.5 Summary to the model investigation of the reactivity of 2-bromooctane with sodium sulfide under various conditions.

It can be concluded that increasing the water content of the solvent system decreases the extent of the reaction and leads to a relatively higher proportion of elimination. Changes in temperature seem to affect the rate of the reaction but do not differentiate between the relative extent of substitution and elimination. The solvent effects were the most significant with aprotic polar solvents giving higher yields of the desired dialkyl sulfide with significant increases in the sulfide to alkene ratio. Table 2.9 compares the original polymer forming conditions and the derived optimised conditions.

Table 2.9: Comparison between the original and the optimised polymer forming reaction.[a]

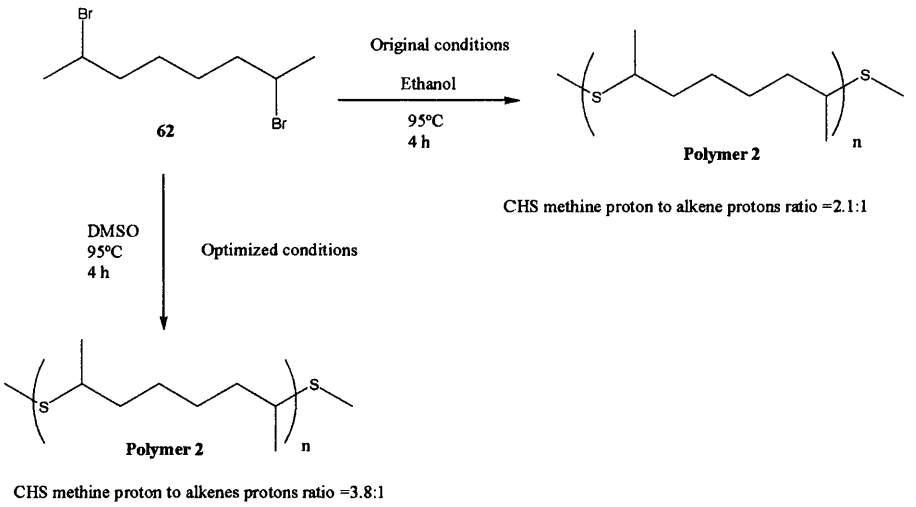
Conditions	Solvent	Time/ h	Temp (°C)	**76** /mol %[b]	**77**/ mol %[b]	**A**/ mol%[b]	S:A	Mass balance
Original	EtOH	4	95	10.9	73.1	11.5	6.4	95.5
Optimised	DMSO	4	95	1.5	89.3	8.0	11.2	97.3

[a] See Scheme 2.26

[b] Yields of 2-bromooctane (**76**), bis-(1-methylheptyl)sulfide (**77**), and octenes **A** (**80-82**) as determined by GC relative to tetradecane as internal standard.

2.12 Application of the optimised conditions to the polymer forming steps.

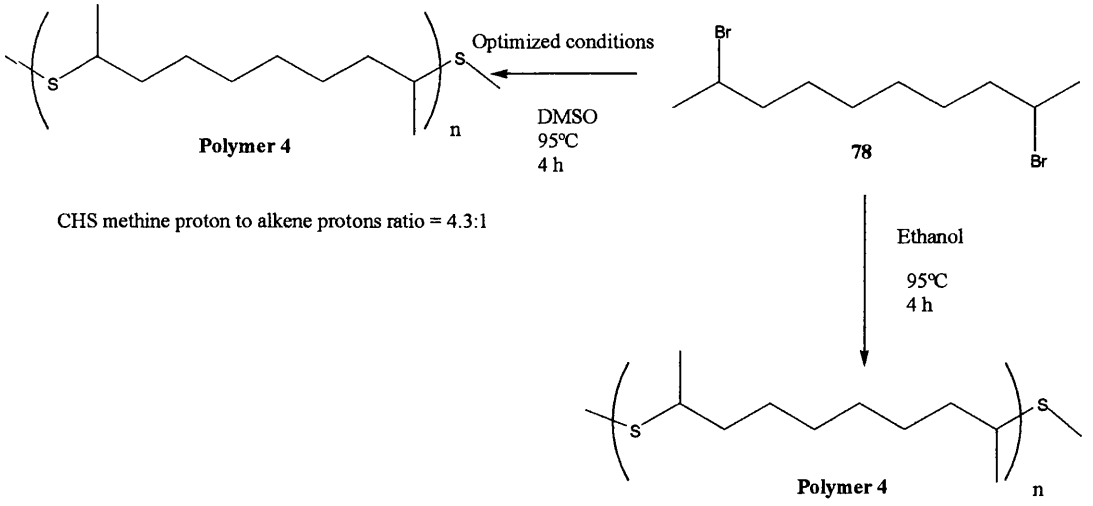
The 2,7-dibromooctane (**62**) was re-synthesised by the established synthetic route and was then reacted with sodium sulfide under the optimised conditions (Scheme 2.29).



Scheme 2.29: Synthesis of **Polymer 2** from 2,7-dibromooctane (**62**) under the optimised polymer forming step: in DMSO, 95 °C for 4 h, with comparison to the initial polymer forming reaction.

The optimised conditions were successful in reducing the extent of elimination, with a rise in the CHS methine proton to alkene protons ratio from 2.1:1 to 3.8:1. Although the elimination cannot be removed completely the value of 3.8:1 represents the relative amounts of the lone methine proton adjacent to sulfur, to the protons on the alkene groups. Considering there are either two or three protons present on the alkenes formed, then in terms of moles there are somewhere between 7.8-11.4 moles of sulfide to every one mole of alkene. It is noteworthy to mention that the actual ratio of amounts is closer to the lower figure of 7.8 due to the dominance of the Zaitsev alkenes, which contain two protons. The number averaged molecular weight (M_n) of the polymer was determined as 670 by GPC.

The 2,9-dibromodecane (**78**) was also re-synthesised by the original derived synthetic route. The hydration step the second time gave a 22 % yield, which is a small improvement on the original 15 % yield. The bromotrimethylsilane substitution step proceeded in 93 % yield, which is similar to the original 95 %. Incidentally, the ratio of 2,9- to 2,8-dibromodecane was 16:1 which is identical to the previous reaction undertaken. The 2,9-dibromodecane was then subjected to the optimised polymer forming conditions (Scheme 2.30).



Scheme 2.30: Synthesis of **Polymer 4** from 2,9-dibromodecane (**78**) by the optimised polymer forming step: in DMSO, 95 °C for 4 h, with comparison to the initial polymer forming reaction.

Unlike the significant decrease in elimination observed for 2,7-dibromooctane (**62**) reported above, the results obtained from the optimised and original conditions for 2,9-dibromodecane (**78**) are fairly similar. A CHS methine proton to alkene protons ratio of 4.3 for the optimised was obtained which is close to the original value of 4.0:1. However, it must be stressed that the model substrate 2-bromooctane (**76**) is more analogous to 2,7-dibromooctane then it is to 2,9-dibromoodecane. It may be possible to obtain more knowledge about the reactivity of 2,9-dibromodecane with sodium sulfide by using 2-bromodecane in a series of model studies. Also, the extent of the elimination for this system was already relatively low and therefore it was decided that no further optimisation would be conducted. The M_n of the polymer was determined as 1330 by GPC.

In all cases the branched polymeric material (**Polymer 2** and **Polymer 4**) synthesised in this chapter existed as oils. All previous polymers isolated at the Centre for Clean Chemsitry were linear polymers and were isolates as solid materials. It is likely that the branched methyl group interrupts the alignment of the polymeric chains and disrupts the amount of van der Waal interactions that can occur. Therefore, reducing the strength of the interaction and subsequently also the physical properties.

2.13 Synthesis of some linear polythiaalkanes.

As previously stated there are several linear polythiaalkanes that have been synthesised at the Centre for Clean Chemistry. In order to have a meaningful comparison between these polymers and the new novel branched analogues synthesised here it was necessary to synthesise the original linear polymers and test them under the exact same chlorination conditions.

Method A (see Section 2.1.1) was utilised for the synthesis of Polymers 3-9, 3-6, 3-12,, and 6-8. Both Methods A and B were used for the syntheses of Polymers 6-6 and 8-8. The yields and the M_n values are shown in Table 2.10.

Table 2.10: Syntheses of some previously established selective linear polythiaalkanes.

Polymer	Yield	M_n
3-9	60	6340
3-6	54	3860
3-12	54	3770
6-6	78[a]	7710
6-6	71	7520
6-8	75	3670
8-8	72[a]	1130
8-8	65	3100

[a]Synthesised by Method B. Otherwise, Method A was used.

2.14 Conclusion for the syntheses of branched polythiaalkanes from secondary dibromides.

A generic regioselective synthetic route from α,Ψ-dienes to ß,Ψ-dibromoalkanes has been formulated and utilised for the synthesis of high purity 2,7-dibromooctane from 1,7-octadiene and the novel 2,9-dibromodecane from 1,9-decadiene.

It has also been discovered that secondary bromides react differently to primary bromides under the existing polymer forming processes of Method B and Method A. More specifically, secondary bromides are less reactive to sodium and lithium thiolates relative to

their primary analogues. This observation suggests that the standard Method A and Method B polymer forming steps proceed *via* an S_N2 mechanism.

A series of investigations using 2-bromooctane and sodium sulfide has shown that secondary bromides will react with sodium sulfide but only in highly polar aprotic solvents (*e.g.* DMSO,DMF) or in protic solvents (*e.g.* ethanol). However, the substitution step proceeds with competing elimination.

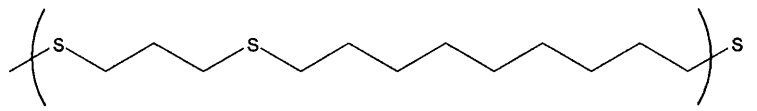
Model studies using 2-bromooctane have led to the development of new conditions for the polymer forming step which was optimised for the reduction of elimination. The best conditions were found to be in DMSO at 95 °C for 4 h.

2.15 Chlorination results using the novel branched Polymer 2 and Polymer 4 as catalysts with comparison to some linear analogues.

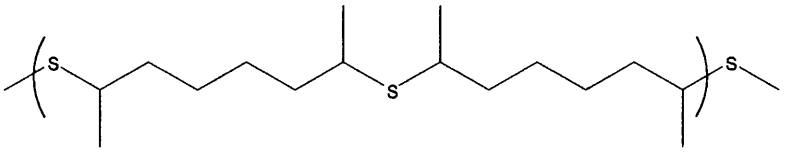
2.15.1 Derivation of standard conditions.

A standard set of conditions was formulated to allow direct comparisons between different catalysts to be made. The amounts of the Lewis acid and the polymer catalyst were derived by analysing a large volume of data from the chlorination of phenols in the presence of linear polythiaalkane catalysts which had been previously conducted at the Centre For Clean Chemistry.[2] The relative amounts used in the most *para* selective results were declared as the most appropriate amounts to use. However, the majority of the reactions previously conducted at the Centre for Clean Chemistry have been carried out on a relatively large scale, typically using 100 mmol of the phenolic substrate (about 10 g for phenol).

In the interest of being more economical with the relatively expensive polymers synthesised here, it was decided to conduct the reactions on a smaller scale. It was decided that 50 mmol of substrate was a fair compromise and was therefore used as the standard amount in this thesis. The amount of the polymer catalysts was obtained by using their pseudo-molecular weight which was defined as the molecular weight of the repeating unit containing two spacing groups, which may or may not be identical. An example is shown in Figure 2.9.



Polymer 3-9: Pseudo molecular weight = 232 ($C_{12}H_{24}S_2$)



Polymer 2: Pseudo molecular weight = 288 ($C_{16}H_{32}S_2$)

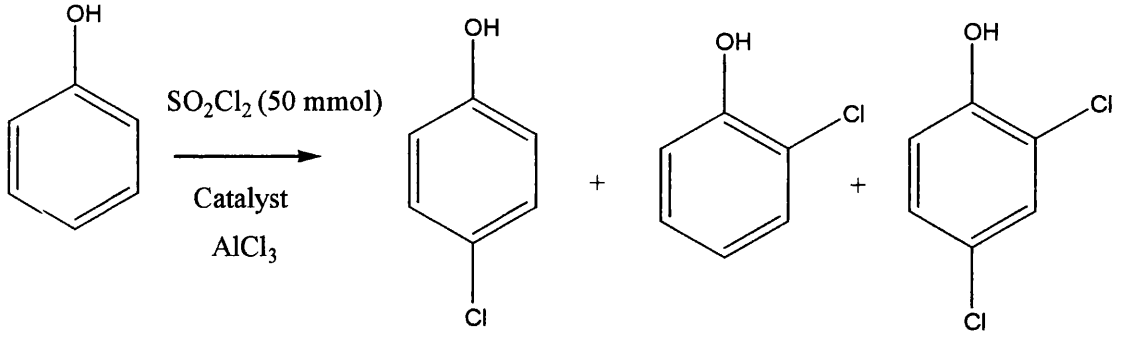
Figure 2.9: Examples of the Pseudo molecular weight values utilised.

The use of the pseudo molecular weight values ensures that the amount of the active sulfide groups can be kept equal even when different polymers are being used.

The derivation of the standard conditions from the previous chlorination results was undertaken in the same manner for all four of the chosen substrates, and the details of the derived standard conditions are reported when relevant.

2.15.2 Chlorination of phenol; standard conditions and baseline results.

The polymeric sulfide materials synthesised in this chapter were tested as selective catalysts for the chlorination of phenol (Scheme 3.31).



P (50 mmol) **PCP** **OCP** **DCP**

Scheme 2.31: The chlorination of phenol.

The standard conditions used for the chlorination of phenol were: phenol (4.706 g, 50 mmol), $AlCl_3$ (0.05 g, 0.375 mmol) and a polymer catalyst (0.284 mmol) were added to a dried 50 mL round bottomed flask. The flask was flushed with nitrogen. Freshly distilled sulfuryl chloride (4.4 mL, 55 mmol) was added slowly over 2 h *via* a pressure equalising

dropping funnel. The reaction was allowed to proceed a further two h. The mixture was then quenched with water (20 mL). The organic components were then extracted with ether (3 x 30 mL). The ether layers were removed and combined then dried over $MgSO_4$ overnight. The drying agent was filtered and the solvents were removed by rotary evaporation. The crude product was weighed and then analysed by quantitative GC.

The baseline results for the chlorination of phenol in the absence of a sulfide catalyst are reported in Table 2.11.

Table 2.11: Baseline results for the reaction of phenol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	**OCP/ mol %** [b]	**P/ mol %** [b]	**DCP/ mol %** [b]	**PCP/ mol %** [b]	***p:o* ratio**	**Mass balance**
-	21.1	8.2	0.7	63.7	3.0	93.7
$AlCl_3$	17.1	10.7	1.0	70.1	4.1	98.9

[a] Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (0.375 mmol).

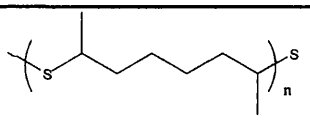
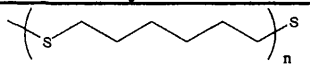
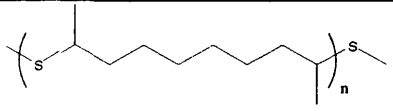
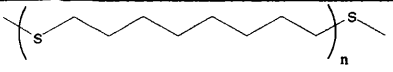
[b] See Scheme 2.31

As indicated by Table 2.11 the baseline results were conducted in the absence of any sulfide catalyst and were conducted with and without a Lewis acid catalyst. The Lewis acid catalyst was in this case aluminium chloride. In both cases a relatively low *p:o* ratio was obtained: 3.0 in the absence of a Lewis acid and a mild improvement to 4.1 with the inclusion of aluminium chloride. In both cases the amount of the remaining starting material was high, with around 10 % being accounted for at the end of the reaction. For the reaction in the absence of the Lewis acid catalyst it is apparent from the mass balance that only about 94 % of the material was accounted for. Therefore, around 6 % of material was lost. The aqueous phases were re-extracted in the hope of obtaining the remaining material but only a negligible amount of material was obtained. New GC solutions were made up and quantitative GC was once again conducted, but the result obtained was essentially identical to that shown in Table 2.11. Even though these two attempts were unsuccessful in recovering more material in this case, the protocol was used as a standard for attempting to recover lost material and was employed when a mass balance of below 95 % was obtained during the remainder of the research.

2.15.3 Chlorination of Phenol with Polymer 2 and Polymer 4, with comparison to their linear analogues.

The standard reaction conditions as described in Section 2.15.2 were then applied with a range of different polymeric sulfide catalysts, and the results are given in Table 2.12.

Table 2.12: Chlorination of phenol with sulfuryl chloride in the presence of branched polythiaalkanes **Polymer 2** and **Polymer 4** with comparison to some linear polymers.[a]

Catalyst	P/ Mol %[b]	OCP/ mol %[b]	PCP/ mol %[b]	DCP/ mol %[b]	*p:o* ratio	Mass balance
 **Polymer 2**	10.5	10.0	72.4	1.0	7.2	93.9
 Polymer 6-6	0.3	12.0	84.1	2.0	7.0	98.4
 **Polymer 4**	5.2	10.3	81.3	1.0	7.9	97.8
 Polymer 8-8	3.3	15.7	78.0	1.2	5.0	98.2
Polymer 3-9	6.3	9.7	83.3	1.3	8.6	100.6
Polymer 3-6	2.3	8.4	88.5	0.5	10.5	99.7

[a]Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide catalyst (0.284 mmol).

[b] See Scheme 2.31.

Under these conditions in the presence of these polymeric sulfides it appears that the extent of the reaction has been improved with the majority of reactions leaving around 5 % or less of the starting material. However, previous results conducted on a larger scale at the Centre for Clean Chemistry,[2] under otherwise comparable conditions have shown that the reaction tends to proceed near to completion quite consistently and in most cases very little of the starting material remained (<3 %). In the reactions conducted herein using 50 mmol of phenolic substrate then it has been generally observed that the reaction does not consistently proceed to the same extent as the previous reactions conducted on a 100 mmol scale.[2] The addition of the sulfuryl chloride is conducted slowly over 2 h in a

drop-wise manner. The addition of each individual drop brings about an apparent exothermic reaction and subsequent effervescence. When you move from a larger scale to a smaller scale (*i.e.* from 100 mmol to 50 mmol) the relative quantity of '1 drop' becomes greater, and therefore the relative exothermic effect also becomes more significant. This increased exothermic effect may result in the reduction of the extent of the reaction by two main ways. Firstly, the heat generated may be sufficient to evaporate the volatile sulfuryl chloride (bp = 68-70°C) and secondly, the relatively large amount of HCl and SO_2 gas produced, spontaneously leaves the vessel and the flow generated may also carry some sulfuryl chloride with it.

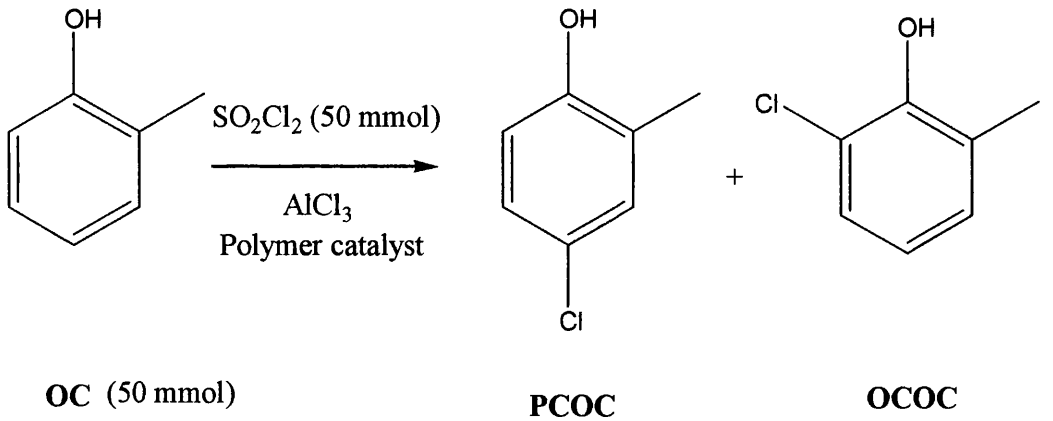
Table 2.12 shows that **Polymer 2** performed in a very similar way to its linear analogue Polymer 6-6 with selectivities of 7.2 and 7.0 respectively. **Polymer 4** seems to be more selective than its linear equivalent with selectivities of 7.9 and 5.0 obtained respectively. In the presence of the two branched polymers the reaction proceeds with selectivities approximately twice as great as in the absence of any catalyst (baseline). The linear Polymers 3-6, and 3-9 were chosen for comparison due to their highly selective manner previously observed for the chlorination of phenol at the Centre for Clean Chemistry.[2] Not surprisingly under these conditions they out-perform the two branched polymers, with the highest selectivities of 10.5 and 8.6.

2.15.4 Chlorination of *o*-cresol; standard conditions and baseline results.

The standard conditions were derived for *o*-cresol (Scheme 2.32) as described above in Section 2.15.1 and are reported below.

o-Cresol (5.410 g, 50 mmol), $AlCl_3$ (0.05 g, 0.375 mmol) and a polymer catalyst (0.284 mmol) were added to a dried 50 mL round bottomed flask. The flask was flushed with nitrogen. Freshly distilled sulfuryl chloride (4.4 mL, 55 mmol) was then added slowly over 2 h *via* a pressure equalising dropping funnel. The reaction was allowed to proceed a further 2 h before being quenched with water (20 mL). The organic components were then extracted with ether (3 x 30 mL). The ether layers were removed and combined then dried over $MgSO_4$ overnight. The drying agent was then filtered and the solvents were removed by rotary evaporation. The crude product was weighed to a constant mass and then analysed by quantitative GC.

The baseline results for the chlorination of *o*-cresol in the absence of any sulfide catalyst are reported in Table 2.30.



OC (50 mmol) **PCOC** **OCOC**

Scheme 2.32: The chlorination of *o*-cresol.

Table 2.13: Baseline results for the chlorination of *o*-cresol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

$AlCl_3$ (g)	OC mol%[b]	OCOC mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
—	2.0	15.4	78.2	5.1	95.6
0.05	9.6	11.9	75.1	6.3	96.6

[a] Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (0.375 mmol).

[b] See Scheme 2.32.

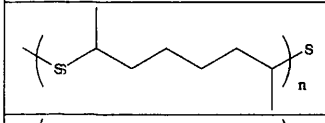
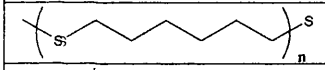
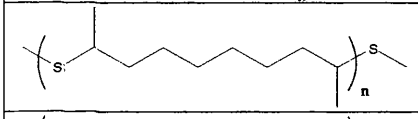
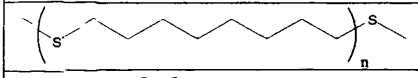
The baseline results for *o*-cresol gave a *p:o* selectivity of 5.1:1 in the absence of $AlCl_3$ and a value of 6.3:1 in the presence of $AlCl_3$. The starting material was almost completely consumed in the absence of any catalyst but around 9.5 % of the *o*-cresol remained at the end of the reaction when the $AlCl_3$ was used. As previously stated, Watson indicated that the Lewis acid does not affect the rate of the reaction but does enhance the selectivity. Indeed in this example the Lewis acid does promote the selectivity from 5.1 to 6.3. The 9.5 % starting material remaining may be due to the exothermic factors mentioned above which are difficult to control or regulate in a consistent manner. The sulfuryl chloride is added at intervals in such a manner that the addition is complete after two h and that the exothermic reaction is best controlled. Ideally this would be done by a regular addition of a regular volume at regular intervals over the 2 h period. However, in practice the initial additions tend to give rise to a more exothermic response, and therefore a smaller volume is added at the start of the reaction and the initial reactions require more time to cool before subsequent additions. This initial slow addition must therefore be compensated by a quicker addition towards the end of the reaction in which there appears to be a less exothermic response. This irregularity in the mode of addition is more problematic on a

smaller scale and may result in the increased amount of remaining starting material observed here. Specifically, it appears that the addition is more exothermic in the presence of the Lewis acid explaining the reduced completion of the reaction observed in the presence of $AlCl_3$ under these conditions.

2.15.5 Chlorination of *o*-cresol with Polymer 2 and Polymer 4.

The standard reaction conditions as described in Section 2.15.4 were then applied with a range of different polymeric sulfide catalysts, and the results are given in Table 2.14.

Table 2.14: Chlorination of *o*-cresol with branched polythiaalkane **Polymer 2** and **Polymer 4** with comparison to some linear polymers.[a]

Catalyst	OC mol%[b]	OCOC mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
	5.6	3.8	89.5	23.6	98.8
	1.5	6.0	91.9	15.3	99.4
	2.6	4.1	93.8	22.9	100.5
	6.7	9.9	78.7	7.9	95.3
Polymer 3-6	10.5	1.5	87.2	58.1	99.2
Polymer 3-9	11.1	3.7	83.2	22.5	98.0
Polymer 3-12	9.9	11.6	77.5	6.7	99.0

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide catalyst (0.284 mmol).

[b] See Scheme 2.32.

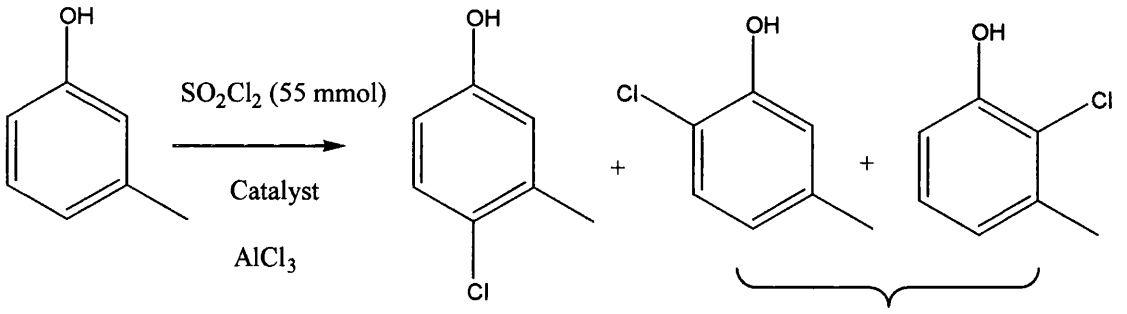
Table 2.14 shows that the two branched polymers gave rise to higher selectivities than their linear equivalents. Both the polymers gave rise to a selectivity value of around 23 which is approaching four times the selectivity value obtained in the baseline results. The linear Polymers 3-6, 3-9, and 3-12 were once again chosen due to their previously observed high selectivities for the substrate. Polymer 3-6 showed that it performed excellently under these conditions to give a staggering *p:o* ratio of 58.1. Polymer 3-9 also performed in a selective manner with a selectivity value of 22.5, but Polymer 3-12 acts as a poor catalyst under these conditions and gives a relatively low selectivity of 6.7. In previous results conducted at the Centre for Clean Chemsitry[2] it has been reported that the linear polymers

used here have all given high *p:o* ratios (>20) under certain conditions. However, that does not mean that they will certainly be selective catalysts under the specific conditions used here. It has been shown that the degrees of selectivities obtainable for a specific catalyst vary considerably depending on the specific reaction conditions, *i.e.* the amount of catalyst, amount of Lewis acid, temperature etc. Carrying out the reactions under the same conditions tells us instantly which catalysts are the most selective under these conditions with the most selective catalysts probably having the most potential as selective catalysts in general. However, it is conceivable that selective catalysts (like Polymer 3-12) can appear to have a low potential as a selective catalyst under a specific set of conditions, but can perform in a highly selective manner under a different set of conditions. It must also be stressed that ultimately a catalyst that results in high selectivity under a range of conditions is more desirable, particularly a catalyst that can maintain its high selectivity when used in small amounts, also with small amounts of the Lewis acid co-catalyst.

2.15.6 Chlorination of *m*-cresol; standard conditions and baseline results.

The standard conditions were derived for *m*-cresol (Scheme 2.33) as described above in Section 2.15.1 and are reported below.

m-Cresol (5.410 g, 50 mmol), $AlCl_3$ (0.25 g, 1.875 mmol) and a polymer catalyst (0.403 mmol) were added to a dried 50 mL round bottomed flask. The flask was flushed with nitrogen. Freshly distilled sulfuryl chloride (4.4 mL, 55 mmol) was added slowly over 2 h *via* a pressure equalising dropping funnel. The reaction was then allowed to proceed for a further 2 h. In some experiments where the reaction mixture solidified the solid was melted using a hot air blower and the mixture was allowed to continue stirring until the end of the 2 h. On some occasions the mixture required melting multiple times (up to 4 times). The mixture was then quenched with water (20 mL). The organic components were then extracted with ether (3 x 30 mL). The ether layers were removed and combined then dried over $MgSO_4$ overnight. The drying agent was then filtered and the solvents were removed by rotary evaporation. The crude product was weighed until constant mass and was then analysed by quantitative GC.



MC (50 mmol) **PCMC** **OCMC**

Scheme 2.33: The chlorination of *m*-cresol.

Baseline results for the chlorination of *m*-cresol with sulfuryl chloride in the absence of a sulfide catalyst are reported in Table 2.15.

Table 2.15: Baseline results for the chlorination of *m*-cresol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	MC/ mol %[b]	OCMC/ mol %[b,c]	PCMC/ mol %[b]	*p:o* ratio	Mass balance
-	8.7	12.5	78.3	6.3	99.5
$AlCl_3$	14.2	10.0	75.8	7.6	100.0

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (1.875 mmol).

[b] See Scheme 2.33.

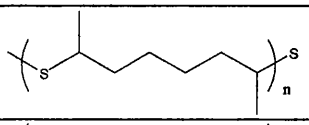
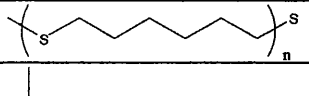
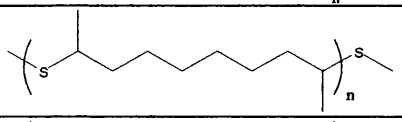
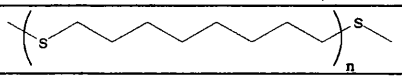
[c] Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

Table 2.15 shows a familiar trend involving enhancement in the *p:o* ratio with the application of a Lewis acid catalyst. In this case only a mild enhancement from 6.3 to 7.6 is observed. More notably, there was once again more starting material remaining when the $AlCl_3$ was used and this is probably due to the reasons described for *o*-cresol.

2.15.7 Chlorination of *m*-cresol with Polymer 2 and Polymer 4.

The standard reaction conditions as described in Section 2.15.6 were then applied with a range of different polymeric sulfide catalysts, and the results are given in Table 2.16.

Table 2.16: Chlorination of *m*-cresol with branched polythiaalkane **Polymer 2** and **Polymer 4** with comparison to some linear polymers.[a]

Catalyst	MC/ mol %[b]	OCMC/ mol %[b,c]	PCMC/ mol %[b]	*p:o* ratio	Mass balance
	3.3	5.5	89.3	16.2	98.1
	9.0	3.8	87.3	23.0	100.1
	3.3	5.7	91.4	16.0	100.4
	4.9	3.9	89.9	23.1	98.7
Polymer 6-8	3.2	5.0	90.7	18.1	98.9

[a]Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the presence of $AlCl_3$ (1.875 mmol) and a polymeric sulfide catalyst (0.403 mmol).

[b] See Scheme 2.33

[c] Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

Table 2.16 shows that both the branched polymers perform in a very similar way giving rise to around 90 % of the desired PCMC in a selectivity of around 16 which is more than twice as selective as the baseline results. Conversely to the trend observed when *o*-cresol was the substrate the direct linear analogues actually out-perform the branched polymers with higher selectivities values in the region of 23. The reason for the reversal of this trend is unknown. Polymer 6-8 performs intermediately to the branched and the other linear polymers under these conditions with a *p:o* ratio of around 18.

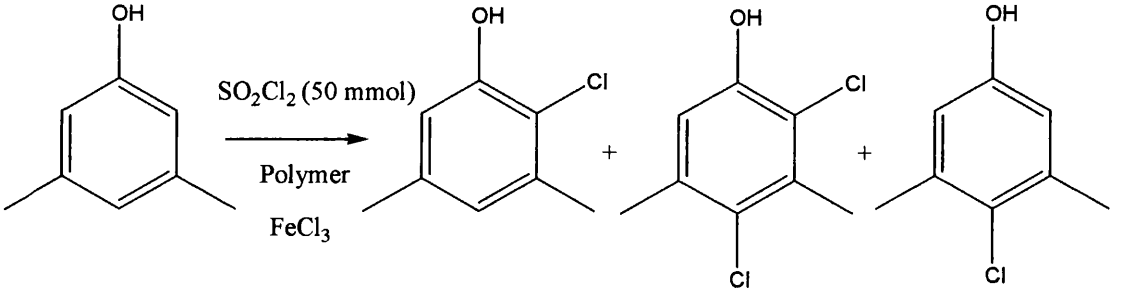
2.15.8 Chlorination of *m*-xylenol; standard conditions and baseline results.

The standard conditions were derived for *m*-xylenol (Scheme 2.34) as described above in Section 2.15.1 and are reported below.

From previous reactions conducted at the Centre for Clean Chemistry,[2] it was apparent for this substrate that higher *para* selectivities were obtained in the presence of $FeCl_3$ as opposed to $AlCl_3$ which was used for phenol, *o*-cresol and *m*-cresol. Previous results[2] also showed that the chlorination of *m*-xylenol is more sensitive to the catalyst and that highly selective results can be obtained by the use of very small amounts of catalyst. Very high selectivities were obtained using 0.104 mmol of catalyst for 100 mmol of

phenolic substrate and therefore for the 50 mmol reactions conducted here, 0.052 mmol of catalyst was used.

m-Xylenol (6.104 g, 50 mmol), $FeCl_3$ (0.025 g, 0.154 mmol), tetrachloroethylene (25 mL) and a polymer catalyst (0.052 mmol) were added to a dried 50 mL round bottomed flask. The flask was then flushed with nitrogen. Freshly distilled sulfuryl chloride (4.4 mL, 55 mmol) was added slowly over 2 h *via* a pressure equalising dropping funnel. The reaction was then allowed to proceed a further 2 h. In some experiments where the reaction mixture solidified the solid was melted using a hot air blower and the mixture was allowed to continue stirring until the end of the 2 h. On some occasions the mixture required melting multiple times (up to 5 times). The mixture was then quenched with water (20 mL). The organic components were then extracted with ether (3 x 100 mL). The ether layers were removed and combined then dried over $MgSO_4$ overnight. The drying agent was filtered and the solvents were removed by rotary evaporation. The crude product was weighed until constant mass and then analysed by quantitative GC.



MX (50 mmol) **OCMX** **DCMX** **PCMX**

eme 2.34: The chlorination of *m*-xylenol.

The baseline results for the chlorination of *m*-xylenol with sulfuryl chloride in the absence of a sulfide catalyst are reported in Table 2.17.

Table 2.17: Baseline results for the reaction of *m*-xylenol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	MX/ mol %[b]	OCMX/ mol %[b]	PCMX/ mol %[b]	DCMX/ mol %[b]	*p:o* ratio	Mass balance
-	13.4	9.8	68.6	0.00	7.0	91.8
$FeCl_3$	15.4	10.3	71.1	0.00	6.9	96.8

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $FeCl_3$ (0.154 mmol).

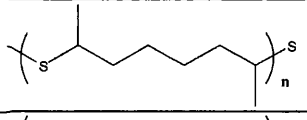
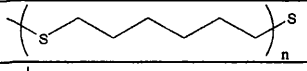
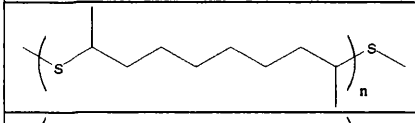
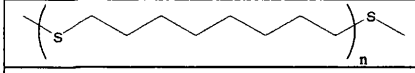
[b] See Scheme 2.34.

According to Table 2.17 it is apparent that under these conditions the chlorination of *m*-xylenol proceeded in a very similar manner with and without the presence of the Lewis acid catalyst. The standard conditions adopted for the chlorination of *m*-xylenol involves the use of only 25 mg of the Lewis acid catalyst. Previous results[2] carried out within the research group had shown that this small amount of Lewis acid when in the presence of certain polymers can gave rise to very high amounts of the desired *para* product. However, it is apparent from the results here that this amount of $FeCl_3$ in the absence of a sulfide catalyst has a very negligible effect on the chlorination relative to when no Lewis acid was employed.

2.15.9 Chlorination of *m*-xylenol with Polymer 2 and Polymer 4.

The standard reaction conditions as described in Section 2.15.8 were then applied with a range of different polymeric sulfide catalysts, and the results are given in Table 2.18.

Table 2.18: Chlorination of *m*-xylenol with sulfuryl chloride in the presence of branched polythiaalkanes **Polymer 2** and **Polymer 4** with comparison to some linear polymers.[a]

Catalyst	MX/ mol %[b]	OCMX/ mol %[b]	PCMX/ mol %[b]	DCMX/ mol %[b]	*p:o* ratio	Mass balance
	0.0	2.4	94.8	0.0	39.5	97.2
	7.0	4.0	88.1	0.0	22.0	99.1
	5.2	4.4	87.3	0.0	19.8	96.9
	1.8	6.9	86.2	0.9	12.5	95.8
Polymer 6-8	10.4	4.7	84.4	0.0	18.0	99.5

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) and a polymeric sulfide catalyst (0.052 mmol).

[b] See Scheme 2.34.

Table 2.18 indicates that under these conditions it is clear that **Polymer 2** is far more selective than its linear equivalent, with respective selectivities of 39.5 and 22.0. The results show a significant increase in the selectivity, with a yield of the desirable *para* chlorinated product of around 95 %. This value is almost certainly lower than it could be under these conditions due to the low mass balance of material accounted for in this

reaction (97.2 % mass balance) which represents almost 3 % of unaccounted material, the majority of which we can assume would be **PCMX**. The use of **Polymer 4** also resulted in good selectivity and also out-performed its linear equivalent in terms of selectivity.

The impressive selectivity of **Polymer 2** for the chlorination of *m*-xylenol prompted further investigation. Emphasis was placed on attempting to increase the selectivity, but ideally also to reduce the amounts of the polymer catalyst and Lewis acid catalyst employed. As touched upon before the most synthetically/commercially valuable catalysts are the ones that can be effective when used in low amounts and also in the presence of very low amounts of the Lewis acid co-catalyst.

2.15.10 Chlorination of *m*-xylenol using various amounts of Polymer 2.

The reaction was repeated under identical conditions to the standard reactions (Section 2.15.8), except that the amount of **Polymer 2** used was varied. The results are shown in Table 2.19.

Table 2.19: Chlorination of *m*-xylenol with sulfuryl chloride in the presence of various amounts of **Polymer 2**.[a]

Amount of Polymer 2/ mg (mmol)	**MX/ mol %**[b]	**OCMX/ mol %**[b]	**PCMX/ mol %**[b]	**DCMX/ mol %**[b]	***p:o* ratio**	**Mass balance**
60 (0.208)	6.4	4.4	87.8	0.0	20.0	98.6
30 (0.104)	5.6	4.2	89.6	0.5	21.3	99.7
20 (0.069)	2.8	3.3	89.9	0.0	27.2	96.0
15 (0.052)[c]	0.0	2.4	94.8	0.0	39.5	97.2
10 (0.035)	1.8	2.3	95.2	0.0	41.4	99.3
6 (0.021)	1.5	4.6	92.0	0.8	20.0	98.9

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) with various amounts of **Polymer 2**.

[b] See Scheme 2.34.

[c] As first shown in Table 2.18.

It is apparent from the results reported in Table 2.19 for **Polymer 2** that the highly selective result obtained using the original 15 mg of the catalyst is the highest value obtainable. It is noticeable that when more catalyst (20, 30 and 60 mg) was used a drop in the selectivity occurred, indicating that the amount used is above a certain optimum value.

When only 10 mg was used a mild enhancement of the selectivity was observed and a *p:o* ratio of around 41 was apparent. When only 6 mg of the catalyst was used a *p:o* ratio of 20.0 was observed, which still represent a good level of selectivity, particularly so, considering the low amount of catalyst employed. However, the value of 20.0 still represents a significant reduction in the *p:o* ratio and the use of 10 mg of this catalyst was carried forward for further investigations.

2.15.11 Chlorination of *m*-xylenol using 10 mg of Polymer 2, with various amounts of $FeCl_3$.

The use of 10 mg of **Polymer 2** was then used in conjunction with various amounts of the Lewis acid and the results are shown in Table 2.20.

Table 2.20: The chlorination of *m*-xylenol using 10mg of **Polymer 2** in the presence of various amounts of $FeCl_3$.[a]

Amount of $FeCl_3$/ mg	**MX/ mol %**[b]	**OCMX/ mol %**[b]	**PCMX/ mol %**[b]	**DCMX/ mol %**[b]	***p:o* ratio**	**Mass balance**
50	6.6	3.8	88.6	0.0	23.3	99.0
35	3.3	3.0	89.6	0.8	29.9	96.7
25[c]	1.8	2.3	95.2	0.0	41.4	99.3
20	7.6	3.8	87.2	0.0	22.9	98.6
15	14.1	4.1	79.0	0.5	19.3	97.7
10	7.3	3.7	87.4	0.0	23.6	98.4
5	1.5	5.1	91.9	0.9	18.0	99.4
3	5.7	4.7	88.0	0.4	18.7	98.8

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of 10 mg of **Polymer 2** (0.035 mmol) with various amounts $FeCl_3$.

[b] See Scheme 2.34.

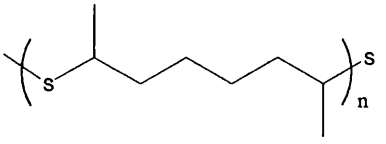
[c] As first shown in Table 2.19.

From Table 2.20 it is immediately apparent that the original selectivity value of 41.4 is the highest and therefore both increasing and decreasing the amount of the Lewis acid gave rise to an unfavourable drop in the selectivity. This indicates that the original 25 mg of catalyst is close to the optimum amount for this system. However, it must be noted that the results at the bottom of Table 2.20, which show a *p:o* ratio of around 18-19, represent a very good level of selectivity when the amounts of catalyst employed is

considered. Only 10 mg of the polymer and 3 or 5 mg of Lewis acid catalyst is required per 50 mmol of substrate to obtain this level of enhancement in the selectivity, which represents approximately a 2.5 times enhancement in the selectivity relative to the baseline values.

2.15.12 Conclusion to the chlorination of phenols using Polymers 2 and 4 as catalysts.

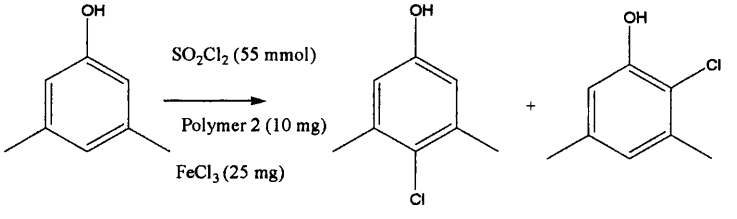
Polymer 2 and **Polymer 4** proved to be effective catalysts for the chlorination of phenol, *o*-cresol, *m*-cresol and *m*-xylenol. Significant increases in *para* selectivity relative to the baseline results were observed in all chosen substrates. More significantly, with the exception of *m*-cresol, the branched polymers out performed their direct linear analogues. The *p:o* ratios obtainable with the branched polymers (particularly **Polymer 2**, Figure 2.8) become greater along the series from the non-substituted phenol through the monosubstituted cresols to the disubstituted xylenol. This trend may be due to the combined steric effect of both the substrates and the catalysts giving rise to enhanced selectivity towards the more accessible *para* position.



Polymer 2

Figure 2.8: **Polymer 2** shown to be a highly selective catalyst for the chlorination of *m*-xylenol with sulfuryl chloride.

A *p:o* ratio of around 41 and a yield of around 95 % of **PCMX** can be obtained in the presence of only 10 mg (0.035 mmol) of catalyst and 25 mg of Lewis acid for 50 mmol of *m*-xylenol (Scheme 2.35).



MX (50 mmol) PCMX 95.2 % OCMX 2.3 %

41.7 : 1

Scheme 2.35: Highly selective chlorination of *m*-xylenol (50 mmol) with sulfuryl chloride (55 mmol) catalysed by **Polymer 2** (10 mg) in the presence of co-catalyst $FeCl_3$ (25 mg, 0.154 mmol).

2.16 General method for the analysis of polymeric material by GPC.

2.16.1 Determination of λ max values by UV spectroscopy.

2.16.1.1 Sample preparation.

Approximately 10 mg of material was dissolved in 10 mL of analytical grade dichloromethane. The solutions were filtered prior to running the spectrometer. Analytical DCM was used as the baseline.

2.16.1.2 Instrument specification.

Instrument: Philips PU 8720 UV/Vis spectrophotometer.
Scan: 200-400 nm.
Bandwidth: 2.0 nm.
Baseline: Analytical grade DCM.

2.16.1.3 Results of UV spectroscopy.

The polystyrene standards and the aromatic containing polymers (see Chapter 4) absorbed strongly at and around 250 nm. The aliphatic thiapolymers all absorbed at and around 238 nm.

2.16.2 GPC analysis; sample preparation.

Samples were made up to contain approximately 50 mg of material in 2 mL of analytical grade DCM. The solution was filtered and cooled in ice prior to injection.

2.16.3 Chromatographic conditions.

Column: Plgel 2 x 30cm (pore size 10^2 and 10^3 Å), 10 microns. Combined MW range 500-20000.
Solvent: Analytical grade DCM, cooled externally in ice.
Flow-rate: 0.7ml/min.

Detector: UV. Set at 250 nm for standards and aromatic containing thiapolymers, and at 238 nm for aliphatic thiapolymers.

Injection volume: 20 µL.

Integrator: Milton Roy CI4000

Pump: Milton Roy ConstaMetric 3000.

2.16.4 Calibration results

Four polystyrene standards ranging from 687-9100 M_n were injected three times each (Table 2.20). The average values were calculated and were used to generate the calibration curve (Figure 2.9).

Table 2.20: Calibration values obtained by GPC analysis of standards.

M_n	Average retention time /min	Retention time/ min			Standard Deviation
		Injection 1	Injection 2	Injection 3	
687	25.62	25.25	25.84	25.76	0.32
2700	24.06	23.89	24.29	24.01	0.21
4075	22.23	22.17	22.34	22.18	0.096
9100	19.57	19.87	19.50	19.33	0.28

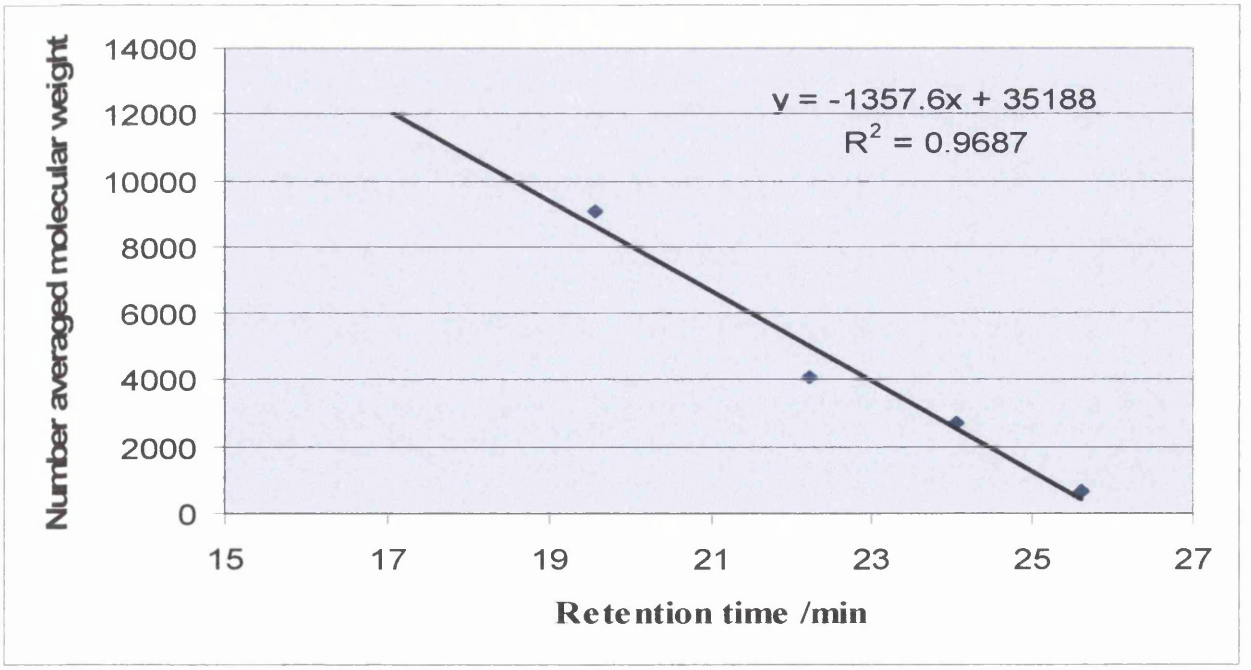


Figure 2.9: Calibration graph for number averaged molecular weight (M_n) of polystyrene standards compared to retention time under conditions described in Section 2.16.3.

2.17 General quantitative GC method.

2.17.1 Sample preparation.

A precisely known amount of the sample (approximately 500 mg) and tetradecane (approximately 500 mg, internal standard) were weighed in a sample vial. The sample was diluted with approximately 30 mL of DCM. The solution (10 μL) was then injected into the GC.

2.17.2 GC Conditions

Instrument: Shimadzu GC-17A.
Column: 15m ZB wax, ID 0.53 μm.
Carrier gas: helium 46 mL/min.
Make up gas: nitrogen 30 mL/min.
Detector gases: hydrogen 60 mL/min, air 300 mL/min.
Injector: 300°C.
Detector: FID. 250°C.
Column start temperature: 40°C.
Start time for ramp: 2 min.
Ramp rate: 20 °C/ min.
Final temperature: 220°C. 5 min duration.

2.17.3 Quantitative calculations

The following equation (Figure 2.10) was used to calculate the response factors for each component.

$$R.F = \frac{\text{Amount sample}}{\text{Amount tetradecane}} \times \frac{\text{Area tetradecane}}{\text{Area sample}}$$

Figure 2.10: Equation for quantitative GC method.

The same equation was rearranged and used to determine the amounts of each component in the test solutions. The value obtained for the weight aliquot was then divided

by the total weight of sample used to make up the solution (around 500 mg) and was then multiplied by the total amount of the crude product obtained in the reaction. The amount obtained in grams was then divided by the molecular weight of the material, then by 50×10^{-3} to compensate for the fact that 50 mmol of substrate was used in the reaction. Finally, the number was multiplied by 100 to obtain the mol % of the component. The procedure was repeated for each reaction component.

2.18 Experimental section.

IR Spectra were obtained using a Perkin Elmer Spectrum One FT-IR spectrometer.

^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz, CPD and DEPT) spectra were obtained using a Brucker AC400 spectrometer with tetramethylsilane as a reference.

Mass spectroscopic analyses were carried out by the EPSRC National Mass Spectrometry Service Centre, Grove Building, University of Wales Swansea. Data for electrospray (ES), electron impact (EI) and chemical ionisation (CI) are stated numerically from the largest detected ion to the smallest detected ion. The abundance of each peak is signified as a percentage relative to the most abundant detected ion. Where conducted, high resolution analysis data is stated after the low resolution data stating firstly the theoretical calculated value (calcd) for the molecular ion peak or the pseudo molecular ion peak followed by the actual value obtained in the analysis (found).

Column chromatography was carried out with silica gel 60A (35-70 μm particle size) or activated alumina (Brockmann I, Standard grade, approx. 150 mesh, 58 Å) as indicated in the individual procedures. TLC analyses were carried out on Whatman aluminium silica gel plates and were visualised initially by UV light followed by development by iodine.

General chemicals were obtained from Aldrich, Fluka, Lancaster and Apollo chemicals and unless otherwise stated were used as supplied.

Tetrahydrofuran was dried by filtration through activated alumina, stirring overnight with calcium hydride and then distilled from sodium benzophenone ketyl.

Sulfuryl chloride was distilled at ambient pressure under an inert atmosphere. Approximately the first 20 % of the volume distilled was discarded and the remaining distillate was obtained as a colourless liquid which was stored in a sealed round bottom flask which was wrapped with aluminium foil to protect it from light and was stored under an inert atmosphere prior to use.

All other solvents stated as dry where dried by standard literature methods.

2.18.1 Attempted synthesis of 2,7-octanediol from 1,7-octadiene *via* acid catalysed hydration.

Crushed ice (5 g) was placed in a conical flask. Concentrated sulfuric acid (15 mL, 285 mmol) was then added slowly and the mixture was allowed to cool. 1,7-Octadiene (4.4 g, 40 mmol) was then added slowly over 30 minutes. Water (70 mL) was added and the mixture was refluxed for 20 minutes and then cooled in ice. The organic components were extracted with ether (50 mL x 2). The ether layers were separated and combined and then washed with aqueous NaOH (5 %, 10 mL x 3). The ether layer was separated and dried over $MgSO_4$. The drying agent was filtered off and the solvent was removed by rotary evaporation to give a thick brown crude oil (4.44 g).

Numerous and varied attempts were made to isolate individual identifiable organic compounds from this reaction. However, this was to no avail. All fractions obtained were sent for ^{1}HNMR, which persistently gave rise to broad mixtures of signals in the region of 0.5- 2.5 ppm, which may be due to the formation of polymeric material (see Section 2.4.1).

2.18.2 Synthesis of 1,6-hexanedial by PCC facilitated oxidation of 1,6-hexanediol.

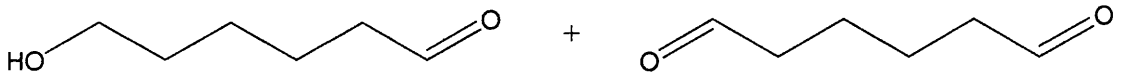
PCC (50 g, 232 mmol) was placed in a round bottom flask fitted with a reflux condenser. Dry dichloromethane (250 mL) was then added. 1,6-Hexanediol (9.18 g, 77 mmol) was dissolved in dry dichloromethane (20 mL) and was then added to the PCC solution. The solution was stirred mechanically for 3 h. Dry ether (200 mL) was then added

and the vessel was shaken for 5 minutes. The organic solvents were then decanted. The insoluble black gum was washed with dry ether (50 mL × 5) until only a black granular solid remained. The organic solvents were then removed by rotary evaporation, and the remaining organic material was passed through a silica column.

The crude oil product (4.83 g) was obtained. The crude product was then distilled under reduced pressure at 16 mmHg. One fraction (1.26 g) distilled at 95-102°C was obtained as a thick oil. NMR confirmed that this fraction was mixture of 1,6-hexanedial and 6-hydroxyhexanal. A second fraction (1.02 g) distilled at 145-157°C was confirmed as 6-hydroxyhexanal (with trace amounts of the desired dial) by NMR analysis. Lit.[27] 145°C at 18 mmHg.

Characteristics of fraction 1-

Mixture of 1,6-Hexanedial and 6-hydroxyhexanal



^{1}H-NMR ($CDCl_3$) δ 1.29-1.65 (complex mixture of aliphatic proton signals from title compounds), 2.40 (m, CH_2CH_2C=O) , 3.65 (t, J = 6.5 Hz, CH_2COH), 9.80 (s, *H*CO). ^{13}C-NMR ($CDCl_3$) δ *1,6-Hexanedial-* 22.0 (C=OCH_2CH_2), 44.1 (C=OCH_2CH_2), 203.3 (C=O). *6-Hydroxyhexanal-* *^{13}C-NMR* ($CDCl_3$) δ 22.1 (O=CCH_2CH_2) 25.2 ($HOCH_2CH_2CH_2$), 33.3 ($HOCH_2CH_2$), 43.9 (O=CCH_2), 62.8 (HOC), 202.6 (O=C). FTIR (neat) *v* 3400 (OH broad str), 1722 (C=O str).

6-Hydroxyhexanal

^{1}H-NMR ($CDCl_3$) δ 1.25 (2H, m, $CH_2CH_2CH_2CH_2C$=O), 1.50 (2H, m, CH_2CH_2COH), 1.60 (2H, m, O=C$CH_2CH_2CH_2$), 2.40 (2H, m, O=CCC_2), 3.50 (2H, t, J = 6.5 Hz, CH_2COH), 9.80 (1H, s, CHO). ^{13}C-NMR ($CDCl_3$) δ 22.1 (O=CCH_2CH_2), 25.2 ($HOCH_2CH_2CH_2$), 33.2 ($HOCH_2CH_2$), 43.9 (O=CCH_2), 62.8 (OHC), 202.47 (O=C). FTIR (neat) *v* 3405 (OH broad str), 1723 (C=O str).

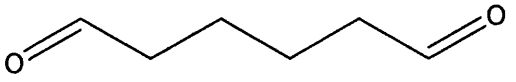
2.18.3 Attempted synthesis of 1,6-hexanedial by the Swern oxidation of 1,6-hexanediol.

At -60°C (chloroform/cardice) dry dichloromethane (250 mL) was added to a three-necked 1 litre round-bottomed flask equipped with an overhead mechanical stirrer, a

calcium chloride drying tube and a septum with a N_2 supply. Oxalyl chloride (20 mL, 220 mmol) was added and was stirred for 5 minutes. Dry dimethyl sulfoxide (40 mL, 480 mmol) was then added slowly over 30 minutes. 1,6-Hexanediol (11.18 g, 100 mmol) was added in a minimum amount of dichloromethane and stirred for 1 h. Triethylamine (70 mL) was then added and the vessel was allowed to warm to room temperature. The organic material was then washed with water (50 mL), saturated NaCl solution (50 mL), HCl solution (50 mL, 1 %), 5 % Na_2CO_3 (50 mL) solution and finally with water (50 mL) once again. All aqueous phases were re-extracted with dichloromethane (25 mL), and the organic phases were combined. The organic phases were dried over $MgSO_4$ for 3 minutes. The drying agent was filtered off and then the solvents were removed by rotary evaporation.

An oily colourless crude product (2.72 g) was obtained. NMR of the crude product confirmed that oxidation had occurred, but the product was a complicated mixture including signals for the starting material.

The experiment was conducted as above only on a smaller scale, with excess DMSO. The amounts used were as follows: dry dimethyl sulfoxide (125 mL), dry dichloromethane (285 mL), 1,6-hexanediol (5.91 g, 50 mmol), oxalyl chloride (13.4 mL, 150 mmol) and triethylamine (40 mL, 300 mmol). After work-up a crude colourless oil (5.10 g, 89 %) was obtained. The crude product was sent for NMR analysis and appeared to be primarily 1,6-hexanedial, with impurities which were probably polymeric (see Section 2.4.3).

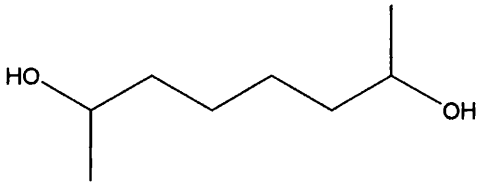


^{1}H-NMR ($CDCl_3$) δ 1.58 (4H, t, J = 6.5, O=CHCH$_2$*CH$_2$*), 2.40 (2H, m, CH$_2$C*H$_2$*HC=O), 9.80 (1H, s, *H*CO).^{13}C-NMR ($CDCl_3$) δ 23.3 (C=OCH$_2$*C*H$_2$), 44.2 (C=O*C*H$_2$CH$_2$), 202.3 (C=O).

2.18.4 Synthesis of 2,7-octanediol by the initial Swern-oxidation of 1,6-hexanediol directly followed by a Grignard reaction of 1,6-hexanedial with methylmagnesium bromide.

Dry dimethyl sulfoxide (125 mL), dry dichloromethane (285 mL) and 1,6-hexanediol (5.91 g, 50 mmol) were mixed together in order to dissolve the diol. The solution was then added to a three-necked 1 litre round-bottomed flask equipped with an overhead mechanical stirrer a calcium chloride drying tube and a septum fitted with a N_2 supply. The flask was cooled externally to -60°C by a dry ice/chloroform mixture. Oxalyl chloride (13.40 mL, 150 mmol) in dry dichloromethane (50 mL) was then added slowly over 30 minutes *via* a dry syringe, and the reaction vessel was then stirred for 2 h. Triethylamine (300 mmol, 40 mL) was added and the vessel was allowed to warm to room temperature. The organic material was then washed with water (40 mL), saturated NaCl solution (50 mL), HCl solution (50 mL, 5 %), water (50 mL), Na_2CO_3 solution (5 %, 50 mL) and finally with water once again. The organic phases were combined and dried over $MgSO_4$ for 2 h. The solution was filtered and the solvents were then removed by rotary evaporation. The oxidation product obtained was dissolved in dry THF (100 mL) and added to a 250 mL round bottom flask, which was cooled to -5 to -10°C by a calcium chloride/ice mixture. The solution was stirred magnetically. Two mole equivalents of MeMgBr (33 mL, 100 mmol, 3M solution in ether) were added slowly over 30 minutes ensuring the temperature did not rise above -5°C. The reaction was allowed to proceed for 30 minutes, and was then left to warm to room temperature before leaving for a further 30 minutes. The organic solution was added to ice (15 g) and was washed with a HCl solution (50 mL, 15 %), the organic phase was separated and the aqueous phase was re-extracted with ether (3 × 20mL). The organic phases were combined and dried with $MgSO_4$. The drying agent was filtered off and the solvents were removed by rotary evaporation.

A crude clear colourless oil (1.79 g, 25 %) was obtained. NMR and mass spectrometry showed that the desired diol was the major component, but there were also other signals present. TLC analysis gave rise to 6 spots. No GC analysis was carried out due to the possibility of high molecular weight components becoming retained on the column.

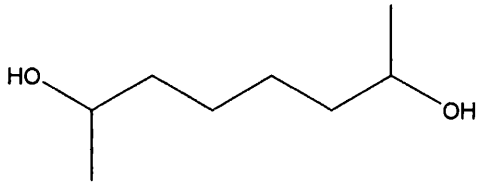


^{1}H-NMR ($CDCl_3$) δ 1.18 (6H, d, J = 6 Hz, CH_3CHOH), 1.30-1.50 (integrates higher that 8H due to overlap with other signals from impurities, m, CH_2CH_2CH(OH)CH_3), 1.90 (2H, s, O*H*, D_2O exchangeable), 3.80 (2H, m, CH_3CHOH).^{13}C-NMR δ 21.2 (CH_3), 23.1 (CH_2CH_2CH(OH)CH_3), 39.6 (CH_2CH_2CH(OH)CH_3), 67.0 (CHOH).
FTIR (neat) *v* 3300 (OH *str*), 2800-2950 (C-H *str*), 2 peaks between 1000-1100 (C-O *str* and O-H *def*). MS ES$^-$ m/z 145 ([M-H]$^-$ 20 %), 129 ([M-OH]$^-$ 100 %), 113 ([M-OH-O]$^-$ 20 %).

2.18.5 Synthesis of 2,7-octanediol from mercury (II) acetate facilitated hydration.

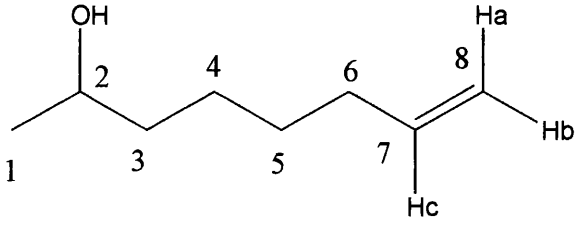
In a 500 mL conical flask, mercury (II) acetate (15.9 g, 50 mmol) was dissolved in water (75 mL) and allowed to stir for 30 minutes. THF (75 mL) was then added to give a fine yellow precipitate, which is probably mercuric oxide. 1,7-Octadiene (2.75 g, 25 mmol) was then added. The yellow precipitate disappeared. The reaction was left to stir for 30 minutes. The conical flask was cooled externally by water. $NaBH_4$ (0.945 g, 25 mmol) in NaOH (75ml, 3M) was then added slowly enough to keep the exothermic reaction under control and keep the temperature bellow 25 °C. The reaction was allowed to proceed for 1 h. Mercury precipitated out of solution. The solution was filtered to remove the mercury which was then isolated (9.89 g, 99 %). NaCl was then added to the mixture to saturate the aqueous phase. Ether (200 mL) was then added. The layers were then separated and the aqueous layer was re-extracted with ether (50 mL). The organic phases were then combined and dried with $MgSO_4$. The drying agent was filtered off and the solvent was removed by rotary evaporation. The crude product was then distilled under reduced pressure (19 mmHg). Any remaining solvent, or 1,7-octadiene was distilled off at ambient temperatures. A clear colourless liquid (0.36 g, 11 %) was distilled off at 76-82 °C (12 mmHg) and was confirmed as the by-product oct-7-en-2-ol by NMR. The title compound was then distilled at 130-140 °C at 12 mmHg (1.72 g, 47 %) and was isolated as colourless clear oil. Lit.[28] 138-140°C at 15 mmHg.

2,7-Octanediol (mixture of diastereoisomers).



^{1}H-NMR ($CDCl_3$) δ 1.18 (6H, d, J = 6 Hz, CH_3CHOH), 1.30-1.50 (8H, m, CH_2CH_2CH(OH)CH_3), 1.90 (2H, s, OH, D_2O exchangeable), 3.80 (2H, m, CH_3CHOH). ^{13}C-NMR δ 22.3 (CH_3), 24.7 (CH_2CH_2CH(OH)CH_3), 38.3 (CH_2CH_2CH(OH)CH_3), 66.9 (CHOH). FTIR (neat) *v* 3300 (-OH *str*), 2800-2950 (C-H *str*) 2 peaks between 1000-1100 (C-O *str* and O-H *def*). MS EI$^+$ m/z 129 ([M-OH]$^+$, 100 %), 111 (Figure 2.6, 10 %), 69 ([C_5H_9]$^+$, 30 %), 56 ([$C_4H_8^+$, 30 %), 45 ([C_3H_9]$^+$, 100 %). CI$^+$ 164 ([M+NH_4]$^+$, 100 %). HRMS EI$^+$ m/z calcd for [M+H]$^+$ 147.1380, found 147.1380.

Oct-7-en-2-ol



^{1}H-NMR ($CDCl_3$) δ 1.18 (3H, d, J = 6 Hz, CH_3CHO), 1.30-1.60 (6H, m, $CH_2CH_2CH_2$CH(OH)CH_3), 1.70 (1H, s, O*H*, D_2O exchangeable), 3.75 (1H, m, CH_3CHOH), 4.95 (1H, appt. d, J = 17 Hz, Ha), 5.03 (1H, appt. d, J = 10 Hz, Hb), 5.80 (1H, m, Hc).^{13}C-NMR ($CDCl_3$) δ 23.9 (C1), 25.6 (C4), 29.3 (C5), 34.1 (C6), 39.6 (C3), 68.5 (C2), 114.8 (C8), 139.3 (C7). FTIR (neat) *v* 3343 (OH *str*), 1641 (C=C *str).* MS EI$^+$ m/z 128 ([M]$^+$, 15 %), 113 ([M-CH_3]$^+$, 20 %), 110 ([M-H_2O]$^+$, 100 %). HRMS EI$^+$ m/z calcd for (M^+) 128.1196, found 128.1193.

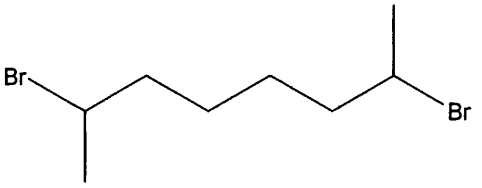
2.18.6 Synthesis of 2,7-dibromoctane; substitution of 2,7-octanediol facilitated by HBr to form 2,7-dibromooctane.

2,7-Octanediol (1.72 g, 11.7 mmol) in a 100 mL 2 necked round bottomed flask fitted with a condenser and a rubber septum was stirred magnetically and cooled externally using an ice bath. Hydrobromic acid (3.9 mL, 23.5 mmol, 48 %) was added *via* syringe. Concentrated sulfuric acid (3.9 mL, 23.5 mmol) was added slowly over 30 minutes *via*

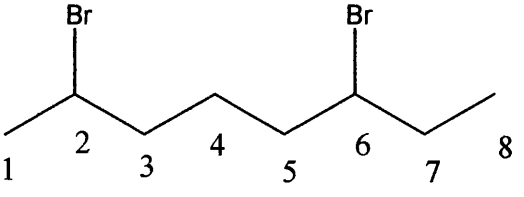
syringe. The mixture was left to react for 24 h, then the reaction was then heated on a steam bath for 4 h. Water (50 mL) and dichloromethane (50 mL) were added. The layers were separated and the aqueous phase was re-extracted with dichloromethane (20 mL). The organic phases were combined and washed with Na_2CO_3 solution (3 x 50 mL, 10 %). The organic phase was separated and dried over $MgSO_4$. The solvents were removed by rotary evaporation to yield a dark brown oil (2.61 g). TLC of the oil using dichloromethane as the elution solvent indicated 2 components, one that remained on the baseline, which is likely to be the brown coloured impurity, and the second component with an RF of 0.77, which was likely to be mainly 2,7-dibromoctane. Column chromatography using dichloromethane gave 1 main fraction (2.43 g, 76 %) of a colourless clear oil. GC analysis showed a ratio of 2,7-dibromooctane to 2,6-dibromooctane of 2.97:1.

The reaction was repeated in the absence of sulfuric acid. 2,7-Octanediol (1.0 g, 6.85 mmol) was used and a mixture of the dibromides (1.80 g, 97 %) was obtained after work up and column chromatography. A ratio of 2,7:2,6 of 1.9 by NMR and 1.4 by GC analysis was determined.

^{1}H-NMR ($CDCl_3$) There is significant overlap of signals in the region of 1.30-1.80 ppm corresponding to various protons within the two regioisomers and therefore no meaningful integrations could be made from this region. However, numerous important signals were qualitatively identified.



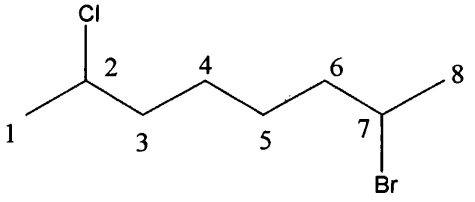
^{1}H-NMR ($CDCl_3$) δ 1.00 (t, J = 7 Hz, C*H*$_3$CH$_2$CHBr), 3.90 (m, CH$_3$CH$_2$C*H*Br) 4.10 (m, CH$_3$C*H*Br).^{13}C-NMR δ *2,7-Dibromooctane* 26.3 (CH$_3$), 27.5 (*C*H$_2$CH$_2$CH(Br)CH$_3$), 41.3 (CH$_2$*C*H$_2$CH(Br)CH$_3$), 52.0 (CHBr).



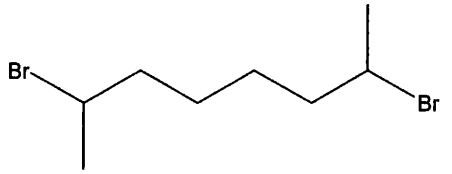
^{13}C-NMR δ *2,6-Dibromooctane* 12.5 (C8), 26.3 (C4), 27.0 (C1), 32.8 (C7), 38.4 (C5), 40.9 (C3), 51.6 (C2), 60.3 (C6). FTIR (neat) *v* 619 (CBr str).

2.18.7 Synthesis of 2,7-dibromooctane; substitution of 2,7-octanediol facilitated by chlorotrimethylsilane and LiBr.

2,7-Octanediol (0.48 g, 3.28 mmol) in a 20 mL round bottom flask was set up with a reflux condenser and a N_2 supply to generate an inert atmosphere. LiBr (1.14 g, 13.15 mmol) was dissolved in dry acetonitrile (14 mL) under N_2. Chlorotrimethylsilane (1.75 g, 16.4 mmol) was then added to the LiBr solution. The resulting solution was added to the 2,7-octanediol. The reaction was allowed to reflux for 24 h. Ether (20 mL) was then added and the organic phase was washed with water (2 × 20 mL), Na_2CO_3 (2×20 mL, 10 %), and finally saturated sodium chloride solution (2 × 20 mL). The organic phase was dried with $MgSO_4$, then filtered, and the solvent was removed by rotary evaporation. A crude product (0.52 g) was obtained. H^1NMR showed that there was still some alcohol remaining. TLC indicated three components. When spotted against the dibromoalkane mixture produced in previous experiments, one component gave an identical Rf and suggest that this was the desired product. Column chromatography was undertaken using ether 25:75 hexane as the elution mixture. One fraction (0.32 g) was obtained, the IR of which showed that there was no hydroxyl group present. GC analysis showed the major product to be 2,7-dibromoalkane, but there was also a significant amount of a by-product present. ^{1}HNMR also showed that 2,7-dibromooctane was the major product and that the major by-product gave a multiplet at 3.9 ppm and a doublet at 1.5 ppm which strongly suggested a secondary chloride. The GC trace also agreed with the possibility of the chloride. GCMS analysis confirmed that the major product was 2,7-dibromooctane and the major by-product was 2-bromo-7-chlorooctane. A ratio of 2,7-dibrooctane to 2-bromo-7-chlorooctane of 3.3:1 was obtained by GC.



^{13}C-NMR δ *2-Bromo-7-chlorooctane* 25.8 (C1), 26.3 (C8), 26.3 (C4), 26.5 (C5), 40.5 (C3), 41.0 (C6), 51.6 (C7), 59.1 (C2).



^{13}C-NMR δ *2,7-Dibromooctane* 26.9 (CH_3), 27.5 ($CH_2CH_2CH(Br)CH_3$), 41.3 ($CH_2CH_2CH(Br)CH_3$), 51.6 (CHBr). GCMS EI^+ m/z *2,7-dibromooctane* 193 ([M(2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{81}Br, ^{79}Br)-^{79}Br]$^+$ 30 %), 191 ([M(^{81}Br,^{79}Br)-^{81}Br]$^+$/ [M(2 x ^{79}Br)-^{79}Br]$^+$ 30 %), 111 (Figure 2.6, 95 %), 69 ($C_5H_9^+$, 100 %), 55 ($C_4H_7^+$, 90 %), 41 ($C_3H_5^+$, 80 %). *2-Bromo-7-chlorooctane* m/z 149 ([M(^{37}Cl)-Br]$^+$ 10 %), 147 ([M(^{35}Cl) -Br]$^+$, 5 %), 111 (Figure 2.6, 95 %), 69 ([C_5H_9]$^+$, 100 %), 55 ([C_4H_7]$^+$, 85 %), 41 ([C_3H_5]$^+$, 80 %). GC ratio of 2,7-dibromooctane: 2-bromo-7-chlorooctane = 3.30:1.

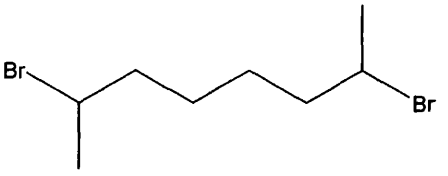
2.18.8 Substitution of 2,7-octanediol facilitated by bromotrimethylsilane and LiBr to synthesise 2,7-dibromooctane.

2,7-Octanediol (1.51 g, 10.27 mmol) was placed in a 100 mL 2 necked round bottom flask fitted with a reflux condenser and a rubber septum. N_2 was flushed in *via* a septum on the reflux condenser and the vessel was kept under an inert atmosphere. LiBr (2.73 g, 41.1 mmol) was dissolved in dry acetonitrile (50 mL) under N_2. Bromotrimethylsilane (6.77 mL, 51.36 mmol) was added *via* a dry syringe. This solution was then added to the 2,7-octanediol *via* a dry syringe. The reaction vessel was heated to 50 °C and allowed to stir. The progress of the reaction was monitored by TLC, until no more starting material or 7-bromooctan-2-ol spot was visible. The reaction was finished after 42 h. Ether (100 mL) was then added and the solution was washed with water (50 mL × 2), $NaHCO_3$ (50 mL, 10 %) and finally saturated NaCl solution (50 mL). All the aqueous phases were re-extracted with ether, and the organic phases were combined and dried over $MgSO_4$. The solvents were then removed by rotary evaporation to give a crude product (1.46 g). TLC suggested some impurities were present. Column chromatography was undertaken using hexane as the eluent. The major component (1.31 g, 47 %) was isolated as a colourless clear oil. Which was shown to be a mixture of 2,7-dibromooctane and 2,6-dibromooctane in a ratio of 5.1:1.

This mixture gave rise to the same characteristics as the similar mixture obtained previously, where the only differences was in the ratio of the two major components (see Section 2.18.7).

2.18.9 Substitution of 2,7-octanediol facilitated by bromotrimethylsilane to synthesise 2,7-dibromooctane in the absence of LiBr.

2,7-Octanediol (1.50 g, 10.3 mmol) was dissolved in dry chloroform (30 mL) and added to a 100 mL 2 necked round bottom flask, which was fitted with a reflux condenser and a rubber septum. The system was flushed with N_2 and kept under an inert atmosphere. Bromotrimethylsilane (4.40 mL, 41.1 mmol) was then added *via* a dry syringe. The reaction vessel was heated to 50°C by a heater and an oil bath, and was stirred magnetically. The mixture was left to react for 92 h. TLC was used to determine if the reaction had gone to completion; the plate was developed by iodine and only one spot was visible. The solution was washed with water (50 mL × 3), a Na_2CO_3 solution (50 mL. 10 %) and finally with a saturated NaCl solution (50 mL). All the aqueous phases were re-extracted and the organic phases were combined and dried over $MgSO_4$. The drying agent was then filtered off and the solvents were removed by rotary evaporation. A crude oily product (3.16 g) was obtained. GC analysis showed that the ratio of 2,7-dibromooctane to 2,6-dibromooctane was 46:1. The GC also showed that there was also starting material present despite the apparent one spot in the TLC analysis of the reaction mixture. TLC of the crude product was undertaken and column chromatography was then carried out. One fraction (2.31 g, 83 %) was obtained as a colourless oil and was almost exclusively 2,7-dibromoocatane.

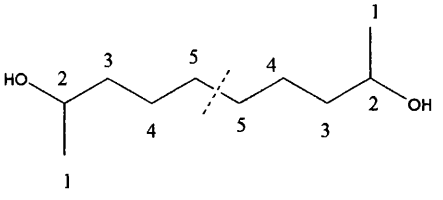


^{1}H-NMR ($CDCl_3$) δ 1.30-1.60 (4H, m, $CH_2CH_2CH(Br)CH_3$), 1.75 (6H, d, J = 6.5 Hz, CH_3CHBr), 1.85 (4H, m, $CH_2CH_2CH(Br)CH_3$), 4.15 (2H, m, CH_3CHBr). ^{13}C-NMR ($CDCl_3$) δ 26.9 (CH_3), 27.5 ($CH_2CH_2CH(Br)CH_3$), 41.3 ($CH_2CH_2CH(Br)CH_3$), 52.0 (CHBr). FTIR (neat) *v* 619 (C-Br str). No OH band. MS m/z EI$^+$ 193 ([M(2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{81}Br, ^{79}Br)-^{79}Br]$^+$ 7 %), 191 ([M(^{81}Br,^{79}Br)-^{81}Br]$^+$/ [M(2 x ^{79}Br)-^{79}Br]$^+$ 30 %), 111 (Figure 2.6, 6 %), 69 ([C_5H_9]$^+$, 100 %), 55 ([C_4H_7]$^+$ 85 %), 41 ([C_3H_5]$^+$, 90 %).

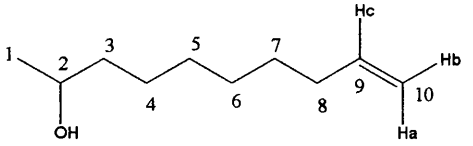
2.18.10 Synthesis of 2,9-decanediol

Mercury (II) acetate (23.05 g, 72 mmol) was added to a 500 mL conical flask and was dissolved in water (70 mL) and allowed to stir for 30 minutes. THF (70 mL) was then added and a yellow precipitate was formed. 1,9-Decadiene (5.01 g, 36 mmol) was then added, and the yellow precipitate disappeared. The reaction was left to stir for 2 h 30 minutes. The flask was cooled externally by water. $NaBH_4$ (2.04 g 54 mmol) in NaOH (70 mL 3M) was added slowly over one hour, ensuring the exothermic reaction was kept below 25°C. The reaction was then stirred vigorously for 3 h, then poured into a separating funnel and left to settle overnight. The mercury layer was removed, and the phases were separated. The aqueous phase was saturated with NaCl and extracted with ether (150 mL). The organic phases were combined and concentrated to a volume of around 50 mL before being washed with water (3×50 mL). The organic phase was dried over $MgSO_4$. The drying agent was filtered off and the solvent was removed by rotary evaporation. A crude product (4.98 g) was isolated. Kuglerohr distillation at 2 mmHg was undertaken to give 3 fractions: fraction 1 (0.52 g) at 25 °C, which is likely to be 1,9-decadiene, fraction 2 (3.21 g) at 115-125 °C, which is dec-9-en-2-ol, and fraction 3 (0.96 g, 15 %) at 156-166 °C which was 2,9-decanediol isolated as a colourless clear oil.

^{1}H-NMR ($CDCl_3$) δ 1.10-1.15 (6H, d, J = 6 Hz, CH_3CHOH), 1.20-1.30 (8H, m, $CH_2CH_2CH_2CH$(OH)CH_3), 1.50 (4H, m, CH_2CH(OH)CH_3), 1.65 (2H, s, OH, D_2O exchangeable), 3.75 (2H, m, CH_3CHOH).



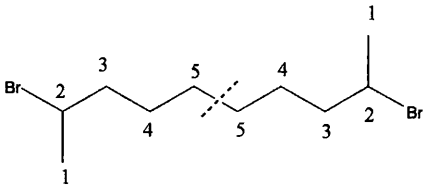
^{13}C-NMR ($CDCl_3$) δ 23.0 (C5), 23.9 (C1), 26.1 (C4), 34.2 (C3), 68.6 (C2). FTIR (neat) *v* 3317 (-OH *str*), 2800-2950 (C-H *str*) 1116, 1076 (C-O *str* and O-H *def*). MS $CI^+(NH_3)$ 192 ($[M+NH_4]^+$,100 %), 174 ($[M]^+$,10 %). HRMS m/z CI^+ calcd for $[M+H]^+$ 175.1691, found 175.1693.



^{1}H-NMR ($CDCl_3$) δ 1.20 (3H, d, J = 6 Hz, CH_3) 1.25-1.50 (10H, $CH(OH)CH_2CH_2CH_2CH_2CH_2CH_2CH{=}CH_2$), 1.60 (1H, s, OH, D_2O exchangeable), 2.10 (2H, m, $H_2C{=}CHCH_2$), 3.80 (1H, m, $CHOH$), 4.95 (1H, appt. d, J = 17 Hz, Ha), 5.05 (1H, appt. d, J = 10 Hz, Hb), 5.70 (1H, m, H_c). FTIR (neat) *v* 3345 (OH *str*), 1641 (C=C *str).* ^{13}C-NMR ($CDCl_3$) δ 23.9 (C1), 26.2, 29.2, 29.5, 29.9 (C4, C6, C5, C7), 34.2 (C8), 39.7 (C3), 68.6 (C2), 114.6 (C10), 139.6 (C9). MS m/z EI$^+$ 155 ($[M\text{-}H]^+$, 10 %), 141 ($[M\text{-}CH_3]^+$, 50 %), 138 ($[M\text{-}OH]^+$, 100 %). HRMS m/z EI$^+$ calcd for $[M\text{-}H]^+$ 155.1430, found 155.1430.

2.18.11 Synthesis of 2,9-dibromodecane

2,9-Decanediol (0.95 g, 5.4 mmol) was dissolved in dry chloroform (20 mL), and was then added to a dry 50 mL 2 necked round bottom flask fitted with a reflux condenser and a rubber septum. The system was flushed with N_2 and maintained under a static N_2 atmosphere. Bromotrimethylsilane (3.34 g, 21.8 mmol) was then added *via* a dry syringe. The reaction vessel was heated to 50 °C by a heater and an oil bath, and was stirred magnetically for 96 h. Dichloromethane (20 mL) was added and the solution was washed with water (20 mL × 3), Na_2CO_3 solution (20 mL, 10 %) and finally with a saturated NaCl solution (20 mL). All the aqueous phases were re-extracted and the organic phases were combined and dried over $MgSO_4$. The drying agent was then filtered off and the solvents were removed by rotary evaporation, to yield crude dark brown oil (1.63 g). TLC analysis was undertaken followed by column chromatography. A colourless clear oil (1.56 g, 95 %) was obtained after column chromatography. The oil was analysed by GC to show it was a mixture of 2,9-dibromodecane and 2,8-dibromodecane in a ratio of 15.5:1.



^{1}H-NMR ($CDCl_3$) δ 1.15-1.55 (8H, $CH_2CH_2CH_2CH(Br)CH_3$), 1.65 (6H, d, J = 6.5 Hz, $CH(Br)CH_3$), 1.78 (4H, m, $CH_2CH(Br)CH_3$), 4.10 (2H, m, $CHBr$). ^{13}C-NMR ($CDCl_3$) δ 26.9 (C1), 28.1 (C4), 29.2 (C5), 41.5 (C3), 52.3 (C2). FTIR (neat) *v* 617 (C-Br str), No OH band. MS EI^+ m/z 221 ([M(2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{81}Br, ^{79}Br)-^{79}Br]$^+$ 100 %), 219 ([M(^{81}Br,^{79}Br)-^{81}Br]$^+$/ [M(2 x ^{79}Br)-^{79}Br]$^+$ 90 %). HRMS CI^+ calcd for $[M+NH_4]^+$ 316.0274, found 316.0274.

2.18.12: Attempted synthesis of poly[sulfanediyl(1,6-dimethylhexane-1,6-diyl)](Polymer 2).

2,7-Dibromooctane (1.01 g, 3.67 mmol) and $Na_2S.9H_2O$ (1.32 g, 5.50 mmol) were added to a 50 mL round bottom flask fitted with a reflux condenser. The reaction vessel was heated to 170°C for 6 h using a silicone oil bath and a heater. The solution was stirred magnetically. DCM (25 mL) was then added followed by water (20 mL), extraction was undertaken, and the phases were separated. The organic phase was dried with $MgSO_4$, filtered and the majority of the solvent was removed by rotary evaporation. Methanol was added in an attempt to precipitate any polymer present. No precipitate was formed. The solvents were removed to give an oil (0.76 g). NMR showed that this is the 2,7-dibromooctane starting material.

2.18.13 Attempted formation of the *semi* branched Polymer 4 by the reaction of 2,7-dibromooctane with 1,6-hexanedithiolate.

1,6-Hexanedithiol (1.15 mL,7.5 mmol) was added into a 50 mL dry flask *via* a dry syringe. The vessel was then flushed with N_2 and was maintained under an inert atmosphere. Dry THF (10 mL) was then added, and the vessel was cooled to -78°C using dry ice and acetone. Butyllithium (2.5M, 6 mL, 15 mmol) was then added *via* a dry syringe over 30 minutes and the mixture was then allowed to stir for 30 minutes. The vessel was then allowed to warm to room temperature. A thick white precipitate was formed. 2,7-Dibromooctane (1.83 g, 6.75 mmol) in dry THF (5 mL) was then added *via* a dry

syringe, and the mixture was stirred overnight. Water (25 mL) was added, and the solution was filtered by suction filtration, but no material was filtered off. TLC analysis of the organic layer indicated 2 components which correlated to the 2,7-dibromooctane and 1,6-hexanedithiol starting materials.

2.18.14 Attempted formation of the *semi* branched Polymer 3 by the reaction of 2,7-dibromooctane with 1,6-hexanedithiolate under reflux conditions.

The above procedure (Section 2.18.13) was followed and after the dithiolate was formed and the dibromooctane was added then the mixture was heated under reflux (75°C) for 92 h. The reaction was worked up as above and once again the TLC analysis indicated two components, which correlated to the 2,7-dibromooctane and the 1,6-hexanedithiol starting materials.

2.18.15 Attempted synthesis of bis-(1-methylheptyl) sulfide.

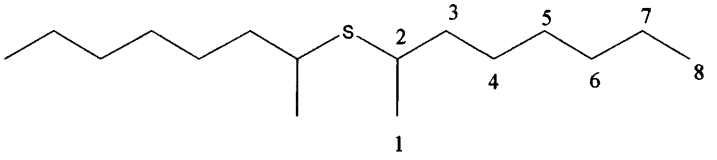
2-Bromooctane (5.02 g, 25.8 mmol) and sodium sulfide (3.10 g, 12.9 mmol) were placed in a 50 mL round bottom flask which was fitted with a reflux condenser. The reaction mixture was heated to 170°C and was then stirred magnetically for 6 h. The solution was then left to cool. Diethyl ether (25 mL) and water (20 mL) were added and extraction was undertaken. The ether layer was dried over $MgSO_4$. The drying agent was filtered off and the solvent was removed to give a crude product (4.87 g). GC and NMR confirmed that this was the 2-bromooctane starting material (97.4 % recovery), with no trace of any sulfide present.

2.18.16 Attempted synthesis of bis-(1-methylheptyl) sulfide using anhydrous sodium sulfide.

The procedure shown above (Section 2.18.15) was followed, but using anhydrous sodium sulfide (1.01 g, 12.9 mmol) instead of the hydrate. The reaction proceeded in an identical fashion with 4.89 g (97.6 %) of 2-bromooctane being recovered.

2.18.17 Synthesis of bis-(1-methylheptyl) sulfide in the presence of ethanol.

The procedure described above was used (Section 2.18.15) but ethanol (25 mL) was also added to the mixture. The mixture was refluxed with an oil bath temperature of 95 °C. The ethanol was removed by rotary evaporation. Water (25 mL) and ether (25 mL) were added and extraction was then undertaken. The ether phase was removed and dried over $MgSO_4$. The drying agent was then filtered off and the ether was removed by rotary evaporation to give a crude product (3.42 g). GC analysis showed that there was only a small amount of 2-bromooctane that remained, with a new product present (2 major peaks in an approximate 50-50 ratio). Reduced pressure distillation was undertaken at 2 mmHg and the remaining 2-bromooctane (0.12 g) was removed at 65-70°C. Another fraction (3.10 g) was distilled at 150-160°C. This fraction was redistilled twice more to give a clear colourless oil (2.56 g, 87 %) which was confirmed as bis-(1-methyl-heptyl) sulfide.



^{1}H-NMR ($CDCl_3$) δ 0.98 (6H, t, J = 6.5 Hz, C*H*$_3$CH$_2$) 1.20-1.70 (26H, protons on C1, C3-C7), 2.80 (2H, m, C*H*S).^{13}C-NMR ($CDCl_3$) δ 14.4 (C8), 21.8 (C1), 23.0, 27.4, 29.6, 32.2 (C4-C7), 37.8 (C3), 39.4 (C2). MS EI$^+$ m/z 258 ($[M]^+$, 15 %), 173 ($[M-C_6H_{13}]^+$, 50 %), 145 ($[M-C_8H_{17}]^+$, 50 %), 43 (C_3H_7, 100 %). FTIR (neat) *v* 722 (possibly C-S). No C-Br str.

2.18.18 Synthesis of poly[sulfanediyl-(1,6-dimethylhexane-1,6-diyl)](Polymer 2).

2,7-Dibromooctane (0.81 g, 2.98 mmol) and ethanol (5 mL) were added to a 25 mL round bottomed flask. Sodium sulfide nonahydrate (0.79 g, 3.28 mmol) was added. A reflux condenser was then attached and the mixture was refluxed for 4 h with an oil bath temperature of 95°C. The ethanol was then removed by rotary evaporation. Water (15 mL) and dichloromethane (20 mL) were added and extraction was undertaken. The aqueous layer was re-extracted with dichloromethane (20 mL). The organic phases were combined and washed with water (3 × 25 mL). The organic phases were then separated and dried over $MgSO_4$. The drying agent was filtered off and the organic phase was then removed by rotary evaporation to give a brown/yellow oily crude product (0.184 g, 44 %). The NMR

showed that there was only a trace amount of the bromide group remaining, with a significant amount of the desired sulfide group. NMR also indicated a significant alkene presence. ^{1}HNMR integrals gave a ratio of CHS methine proton:alkene protons of 2.1:1. The reaction was also carried out under the optimised conditions which differed only in the solvent used. DMSO was used instead of ethanol. The polymer obtained from this reaction differed from the previous one only in the extent of the alkene incorporation. The product of this reaction had a CHS methine proton: alkene protons ratio of 3.8:1.

^{1}H-NMR ($CDCl_3$) δ ***Polymer 2*** 1.00-1.60 (8.76 protons, expected 7), 2.70 (1H, m, CHS). *Zaitsev alkene groups* 5.30-5.45 (CH_3CH=$CHCH_2$, *cis-* and *trans-*).

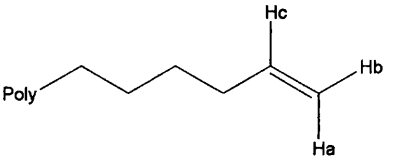
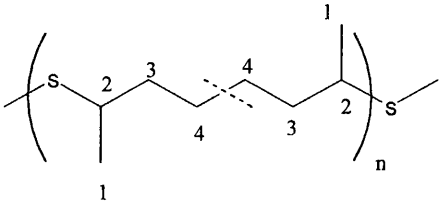


Figure 2.11: Diagram indicating the protons identified on the Hofmann alkene present within **Polymer 2**.

Hofmann alkene group (Figure 2.11*)* δ 4.90 (1H, appt. d, J = 17 Hz, Ha), 5.00 (1H, appt. d, J = 10 Hz, Hb), 5.70 (1H, m, Hc).

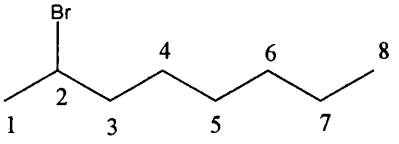


^{13}C-NMR ($CDCl_3$) δ ***Polymer 2*** 22.1 (C1), 27,1, 27.2 (C3, C4), 39.0 (C2). *Most abundant Zaitsev (trans-) alkene group* 125.4 (CH_3CH=$CHCH_2$). 131.5 (CH_3CH=$CHCH_2$). *Least abundant Zaitsev (cis-) alkene group* 124.4 (CH_3CH=$CHCH_2$), 130.7 (CH_3CH=$CHCH_2$). *Hofmann alkene* 114.8 (CH_2=$CHCH_2$), 139.5 (CH_2=$CHCH_2$). FTIR (neat) *v* 731 (possibly C-S). No C-Br str. GPC M_n 680.

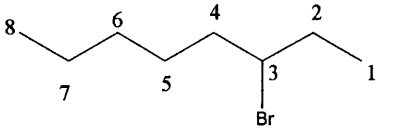
2.18.19 Synthesis of 2-bromooctane

2-Octanol (9.96 g, 76 mmol) and dry chloroform (150 mL) were placed in a dry 3 necked 250 mL round bottomed flask which was fitted with a reflux condenser, sealed with a septum and flushed with N_2. Bromotrimethylsilane (23.51 g, 153 mmol, 19.9 mL) was added *via* a dry syringe. The reaction was heated to 50 °C and stirred magnetically. An

aliquot (1.5 mL) of solution was taken every 24 h, diluted with more chloroform (2 mL) and then washed with water (3x 2 mL), $NaHCO_3$ solution (3 mL, 10 %). The phases were separated using a 1 mL pipette. The organic phase was dried over $MgSO_4$ and the solvent was removed by rotary evaporation. The composition of the resulting oil was initially tested solely by FTIR to monitor the reaction *via* depletion of the large OH stretch at around 3300 cm^{-1}. Towards the end of the reaction the aliquot composition was monitored dually by FTIR and by the more quantitative method of GC analysis. The reaction progress appeared to stop after 144 h. Water (150 mL) was slowly added to the vessel. The reaction mixture was transferred to a separating funnel and extraction was undertaken. The organic phase was washed twice more with water (150 mL) and then with a $NaHCO_3$ solution (150 mL, 10 %).The organic phase was separated and dried over $MgSO_4$, then filtered. The solvent was removed by rotary evaporation to give the crude oil product (13.86 g). TLC analysis was undertaken followed by column chromatography using a silica stationary phase and a 10:1 ether:hexane solvent mixture. A fraction corresponding to 2-bromooctane was isolated (12.21 g, 82.6 %) as a clear colourless oil. GC was used to show that the product was 2-bromooctane (97.3 % purity), with only a small amount of 3-bromooctane formed (2.7 %).



^{1}H-NMR ($CDCl_3$) δ 0.87 (3H, t, J = 6.5 Hz, CH_3CH_2), 1.20-1.60 (8H, m, $CH_2CH_2CH_2CH_2$), 1.70 (3H, d, J = 6.5 Hz,CH_3CHBr), 1.84 (2H, m, $BrCH(CH_3)CH_2$), 4.15 (1H, m CHBr). ^{13}C-NMR δ *2-bromooctane* 14.5 (C8), 22.9 (C7), 26.9 (C1), 27.7, 29.1, 31.7 (C4, C5, C6), 41.6 (C3), 52.3 (C2).



^{13}C-NMR δ 3-*bromooctane* 12.5 (C1), 14.5 (C8), 23.0 (C7), 27.7, 31.7 (C5,C6), 32.6 (C2), 39.2 (C4), 61.03 (C3). FTIR (neat) *v* No OH str, 818 (C-Br str).

2.18.20 Synthesis of poly[sulfanediyl-(1,8-dimethyloctane-1,8-diyl)](Polymer 4)

2,9-Dibromodecane (1.00 g, 3.33 mmol), sodium sulfide nonahydrate (0.88 g, 3.66 mmol) and ethanol (5 mL) were added to a 25 mL round bottomed flask. A reflux condenser was then attached and the reaction was refluxed for 4 h using an oil bath temperature of 95°C. The ethanol was then removed by rotary evaporation. Water (20 mL) and dichloromethane (20 mL) were added and an emulsion was formed. A saturated NaCl solution (40 mL) and DCM (30 mL) were added successfully to remove the emulsion. The phases were separated and the aqueous layer was re-extracted with dichloromethane (20 mL). The organic phases were combined and washed with water (3 × 25 mL), then were separated and dried over $MgSO_4$. The solvents were removed by rotary evaporation to give a clear colourless oily crude product (0.504 g). NMR indicated that only a trace amount of the bromide group remained and instead showed a significant amount of the desired sulfide group, but, also a significant alkene presence. ^{1}HNMR integrals showed a CHS methine proton:alkene protons ratio of around 4:1. The reaction was also carried out under the optimised conditions, which differed only in the solvent used. DMSO was used instead of ethanol. The polymer obtained from this reaction differed from the previous one only in the extent of the alkene incorporation. The product of the DMSO reaction had a CHS methine proton:alkene protons ratio of 4.3:1.

^{1}H-NMR ($CDCl_3$) δ ***Polymer 4*** 1.10-1.60 (10H, expected 9), 2.75 (1H, m, CHS). *Zaitsev alkenes* 5.25-5.45 (CH_3CH=$CHCH_2$, *cis-* and *trans-*).

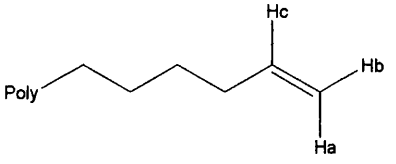
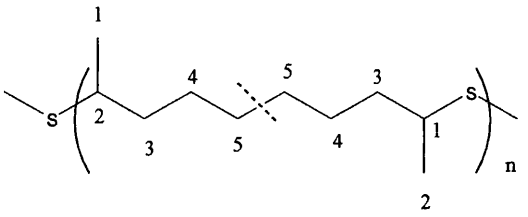


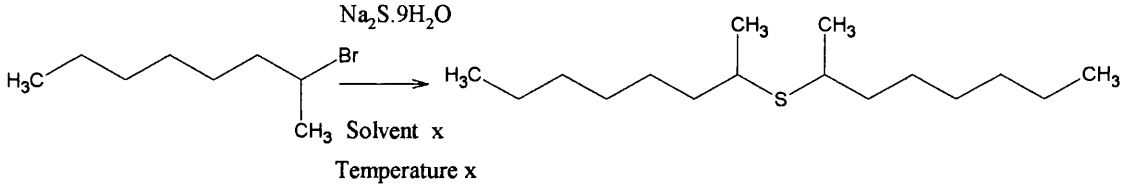
Figure 2.12: Diagram indicating the protons identified on the Hofmann alkene present within **Polymer 4**.

Hofmann alkene group (Figure 2.12) δ 4.90 (1H, appt. d, J = 17 Hz, Ha), 5.00 (1H, appt. d, J = 10 Hz, Hb), 5.80 (1H, m, Hc).



^{13}C-NMR δ ***Polymer 4*** 22.2 (C1), 27.2, 29.8 (C4,C5), 37.5 (C3), 38.9 (C2). Most *abundant Zaitsev (trans-) alkene* group 125.1 ($CH_3CH{=}CHCH_2$), 131.9 ($CH_3CH{=}CHCH_2$). *Least abundant Zaitsev (cis-) alkene group* 124.1 ($CH_3CH{=}CHCH_2$), 131.1 ($CH_3CH{=}CHCH_2$). *Hofmann alkene group* 114.6 ($CH_2{=}CHCH_2$), 139.5 ($CH_2{=}CHCH_2$). FTIR (neat)*v* 725 (possibly C-S). No C-Br str. GPC M_n 1330.

2.18.21 The model reaction of 2-bromooctane with sodium sulfide under various conditions (Scheme 2.36).



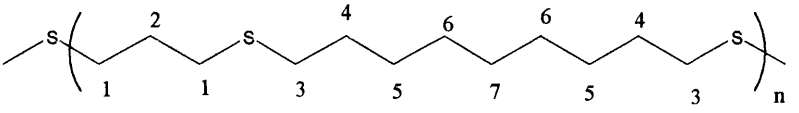
Scheme 2.36: The reaction of 2-bromooctane with sodium sulfide under various conditions.

2-Bromooctane (1.00 g, 5.18 mmol), $Na_2S.9H_2O$ (0.68 g, 2.85 mmol) and the solvent (5 mL) were placed in a 25 mL round-bottomed flask fitted with a reflux condenser. The temperature and the duration of the reaction were varied where appropriate; the values are stated in Section 2.11. The reaction was allowed to cool and was then quenched with water (10 mL). Diethyl ether (10 mL) was then added and extraction was undertaken. The aqueous phase was re-extracted with ether (10 mL) and the organic phases were combined and dried over $MgSO_4$. The drying agent was filtered off and the solution was added to a known amount of tetradecane (internal standard) and was then made up to 50 mL in a volumetric flask and injected into the GC. Rf values for 2-bromooctane were calculated using the synthesised 2-bromooctane (see Section 2.18.19). Bis-(1-methylheptyl) sulfide was isolated by kuglerohr distillation from experiment BRS1 (see Section 2.11) (0.406 g, 61 %) and its Rf value was determined. The Rf values of the octenes were determined from authentic samples and identified by their adjusted retention times and by

the addition to the product mixture in order to determine whether a new component (peak) was visible or if an existing component was enhanced.

2.18.22 Synthesis of poly(sulfanediylpropane-1,3-diylsulfanediylnonane-1,9-diyl) (Polymer 3-9).

The standard Method A procedure was followed and the following amounts were used: 1,3-propanedithiol (2.34 mL, 15 mmol), dry THF (20 mL) butyllithium (2.5M, 12 mL, 30 mmol), 1,9-dibromononane (3.861 g, 13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). After filtration and washing the resulting powder was then removed from any volatile components by heating to 50°C at 2 mmHg for 4 h. The resulting white powder product was obtained (2.11 g, 60 %).



^{1}H-NMR ($CDCl_3$) δ 1.20-1.40 (10H, m, $SCH_2CH_2(CH_2)_5CH_2CH_2S$), 1.50 (4H, m, $SCH_2CH_2(CH_2)_5CH_2CH_2S$), 1.75 (2H, t , J = 7.5 Hz, $SCH_2CH_2CH_2S$), 2.45 (4H, t, J = 7 Hz, $SCH_2CH_2(CH_2)_5CH_2CH_2S$), 2.58 (4H, t, J = 7 Hz, $SCH_2CH_2CH_2S$). ^{13}C-NMR ($CDCl_3$) δ 29.1, 29.3, 29.6, 29.8, 30.7, 31.4, 32.5 (C1-C7).

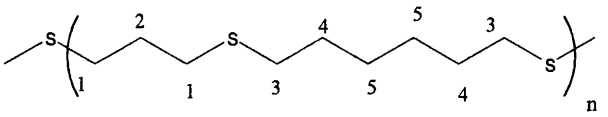
Seven intense peaks correlate to the seven different expected carbon environments. However, due to the very similar frequencies of the observed carbons no attempt has been made to assign them individually, but only to account for their presence. This approach to the assignment also applies to the remainder of the linear polymers synthesised in this chapter, which are reported in the next sections. Several smaller peaks were also present in this case between 29-34 ppm which probably arise form additional carbon environments as a result of the presence of terminal groups.

FTIR (neat) *v* 724 (possibly C-S). No C-Br str. GPC M_n 6340.

2.18.23 Synthesis of poly(sulfanediylpropane-1,3-diylsulfanediylhexane-1,6-diyl) (Polymer 3-6).

The standard Method A procedure was followed and the following amounts were used: 1,3-propanedithiol (2.342 mL, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), 1,6-dibromhexane (3.29 g, ,13.5 mmol) and 1-bromobutane (0.41 g,

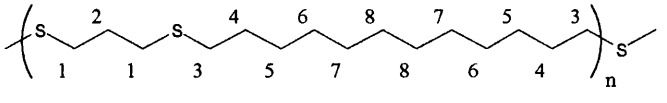
3 mmol). After filtration and washing the powder was then removed from any volatile components by heating to 50 °C at 2 mmHg for 4 h. The resulting white powder product was obtained (1.54 g, 54 %) .



^{1}H-NMR ($CDCl_3$) δ 1.38 (4H, m, $SCH_2CH_2C\mathit{H}_2C\mathit{H}_2CH_2CH_2S$), 1.67 (4H, m, $SCH_2C\mathit{H}_2CH_2CH_2C\mathit{H}_2CH_2S$), 1.90 (2H, m, $SCH_2C\mathit{H}_2CH_2S$), 2.53 (4H, t, J = 7 Hz, $SC\mathit{H}_2CH_2CH_2CH_2CH_2C\mathit{H}_2S$), 2.60 (4H, t, J = 7 Hz, $SC\mathit{H}_2CH_2C\mathit{H}_2S$).
^{13}C-NMR ($CDCl_3$) δ 28.9, 29.8, 29.9, 31.4, 32.5 (C1-C5).FTIR (neat) *v* 726 (possibly C-S). No C-Br str. GPC M_n 3860.

2.18.24 Synthesis of poly(sulfanediylpropane-1,3-diylsulfanediyldodecane-1,12-diyl) (Polymer 3-12).

The standard Method A procedure was followed and the following amounts were used: 1,3-propanedithiol (2.342 mL, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), 1,12-dibromododecane (4.43 g, 13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). After work-up the crude powder was then removed from any volatile components by heating to 50°C at 2 mmHg for 4 h. The final white polymeric powder product was obtained (2.23 g, 54 %).



^{1}H-NMR ($CDCl_3$) δ 1.10-1.40 (16H, m, $SCH_2CH_2(C\mathit{H}_2)_8CH_2CH_2S$), 1.55 (4H, m, $SCH_2C\mathit{H}_2(CH_2)_8C\mathit{H}_2CH_2S$), 1.80 (2H, m, $CH_2C\mathit{H}_2CH_2S$), 2.45 (4H, t, J = 7 Hz, $SC\mathit{H}_2CH_2(CH_2)_8CH_2C\mathit{H}_2S$), 2.60 (4H, t, J = 7 Hz, $SC\mathit{H}_2CH_2C\mathit{H}_2S$).
^{13}C-NMR ($CDCl_3$) δ 29.4, 29.7, 29.9, 30.0, 30.0, 30.1, 31.4, 32.6 (C1-C8) FTIR (neat) *v* 726 (possibly C-S). No C-Br str. GPC M_n 3770.

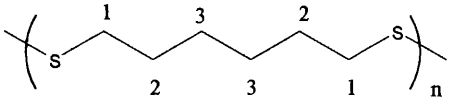
2.18.25 Synthesis of poly(sulfanediylhexane-1,6-diyl) (Polymer 6-6).

By Method B

1,6-Dibromohexane (5.02 g, 20.5 mmol) and $Na_2S.9H_2O$ (7.39 g, 30.8 mmol) were added to a round bottomed flask (25 mL). The flask was heated to 170°C using a heater and stirrer unit and a silicon oil bath. The reaction was allowed to proceed for 6 h. The vessel was allowed to cool and then water (15 mL) was added. The white precipitate was removed by filtration and washed thoroughly with methanol (3 x 30 mL), ether (3 x 30 mL) and hexane (3 x 30 mL). The white powder was then removed from any volatile materials in a vacuum oven (40°C, 1 mmHg) for 24 h. The resulting white powder (1.86 g, 78 %) was then obtained.

Method A

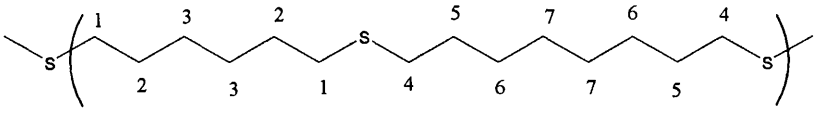
The standard Method A procedure was followed and the following amounts were used: 1,6-hexanedithiol (2.30 mL, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), 1,6-dibromhexane (3.29 g, 13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol) After filtration and washing the powder was then removed from any volatile components by heating to 50°C at 2 mmHg for 4 h. The resulting white powder product was obtained (2.74 g, 71 %). With the exception of trace amounts of different terminal groups the NMR spectra of both products were identical.



^{1}H-NMR ($CDCl_3$) δ 1.35 (4H, m, $CH_2CH_2CH_2S$), 1.50 (4H, m, $CH_2CH_2CH_2S$), 2.45 (4H, t, J = 7 Hz, CH_2S). ^{13}C-NMR ($CDCl_3$) δ 28.4, 29.5, 32.4 (C1,C2,C3).
FTIR (neat) *v* 725 (possibly C-S). No C-Br str. GPC M_n 7520 (Method A product), 7710 (Method B product).

2.18.26 Synthesis of poly(sulfanediylhexane-1,6-diylsulfanediyloctane-1,8-diyl) (Polymer 6-8).

The standard Method A procedure was followed and the following amounts were used: 1,6-hexanedithiol (2.30 mL, 15 mmol) dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), 1,8-dibromooctane (3.67 g,13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). After work-up the crude powder was then removed from any volatile components by heating to 50 °C at 2 mmHg for 4 h. The final white polymeric powder product obtained (2.93 g, 75 %)

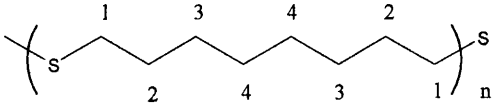


^{1}H-NMR ($CDCl_3$) δ 1.15-1.40 (12H, m, protons on C3, C6, C7), 1.45-1.55 (8H, m, SCH_2CH_2), 2.50 (8H, m, J = 7.5 Hz, SCH_2CH_2) ^{13}C-NMR ($CDCl_3$) 28.5, 29.0, 29.3, 30.3, 30.8, 32.2, 32.3. (C1-C7) FTIR (neat) *v* 723 (possibly C-S). No C-Br str. GPC M_n 3670.

2.18.27 Synthesis of Synthesis of poly(sulfanediyloctane-1,8-diyl) (Polymer 8-8).

The standard Method B procedure was utilised and the following amounts were used: 1,8-dibromooctane (5.01 g, 18.4 mmol) and $Na_2S.9H_2O$ (6.62 g, 27.6 mmol). After work-up the white powder was then removed from any volatile materials in a vacuum oven (40°C, 1 mmHg) for 24 h. The resulting white powder (1.92 g, 72 %) was then obtained.

The standard Method A procedure was followed and the following amounts were used: 1,8-octanedithiol (2.60 mL, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), 1,8-dibromooctane (3.67 g, 13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). After work-up the crude powder was then removed from any volatile components by heating to 50°C at 2 mmHg for 4 h. The final white polymeric powder product obtained (2.81 g, 61 %).



^{1}H-NMR ($CDCl_3$) δ 1.20-1.50 (8H, m, protons on C3, C4), 1.60 (4H, m, SCH_2CH_2), 2.50 (4H, t, J = 7.5 Hz, SCH_2CH_2).^{13}C-NMR ($CDCl_3$) 29.1 (C4) 29.3 (C3), 29.6 (C2), 33.2 (C1).FTIR (neat)*v* 720 (possibly C-S). No C-Br str. GPC M_n 3100 (Method A product), 1130 (Method B product).

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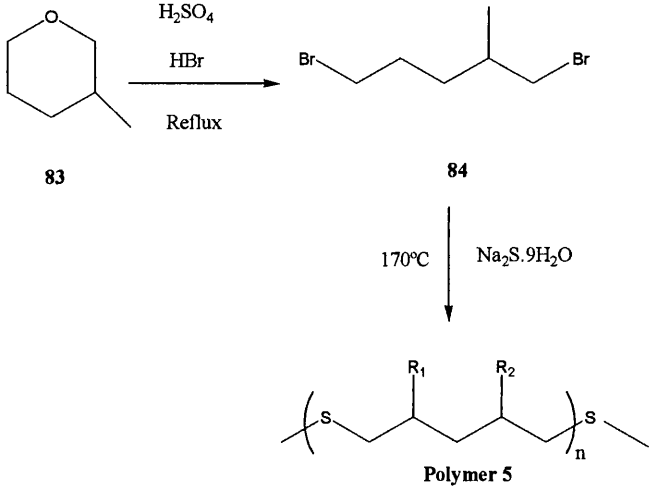
Chapter 3: Syntheses of branched polythiaalkanes from branched primary dibromides and their use as catalysts for the chlorination of phenols.

3.1 Introduction

As reported in chapter 2, competing elimination occurs when secondary dibromides undergo substitution in the presence sodium sulfide. Despite the investigation of various parameters the elimination could not be removed completely. It was decided that one way to bypass this problem was to incorporate the branched (methyl) groups into the polymeric material *via* primary dibromides. To further assess how the level of steric hindrance within the polymer affects the selectivity of chlorination it was required to synthesise a series of dibromides with various degrees of branching to synthesise the equivalent series of polymers. As previously stated, Polymer 6-6 is a highly selective catalyst for the chlorination of phenol. The analogous Polymer 5-5 had not previously been synthesised. Therefore, it was decided that polymers with pentylene repeating units which incorporate various degrees of branching were the desired target molecules. It was originally assumed that by using Method B various polymeric sulfides could be synthesised from various 1,5-dibromopentanes.

3.2 Synthesis of branched Polymer 5 from 1,5-dibromo-2-methylpentane

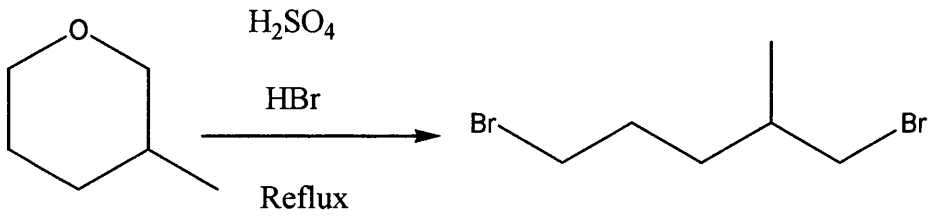
A series of synthetic routes to branched 1,5-dibromopentanes was derived, the first of which is shown in Scheme 3.1.



Scheme 3.1: Synthetic route to **Polymer 5** by the ring opening reaction of 3-methyltetrahydropyran (**83**) to obtain 1,5-dibromo-2-methylpentane (**84**) followed by Method A polymer forming step.

3.2.1 Synthesis of 1,5-dibromo-2-methylpentane.

The first step involves a nucleophilic ring opening and substitution reaction facilitated by hydrobromic acid in concentrated sulfuric acid. The method used by Johnson et al was followed [1](Scheme 3.2).



83 **84**

Scheme 3.2: Synthesis of 1,5-dibromo-2-methylpentane (**84**) by HBr facilitated nucleophilic ring opening of 3-methyltetrahydropyran (**83**).

The reaction involved refluxing the tetrahydropyran (**83**) in the presence of hydrobromic acid and sulfuric acid for 2 h. The reaction was conducted 3 times. Initially using 50 mmol of 3-methyltetrahydropyran and then twice more on a larger scale (100 mmol) in order to obtain a sufficient quantity of material to investigate the polymer forming step.

The reaction products were isolated by reduced pressure distillation and their purity was analysed by GC analysis. The first two experiments resulted in the isolation of relatively impure brown coloured oils (purities of 93.2 and 94.6 %). The crude product of the third reaction carried out was initially passed through a silica column in order to remove the brown colouration and subsequent imuprites and was then subjected to reduced pressure distillation to give a clear colourless oil with a purity value of 99.3 %. These results are summarised in Table 3.1.

Table 3.1: The formation of 1,5-dibromo-3-methylpentane (**84**) from 3-methyltetrahydropyran (**83**).[a]

Experiment	Reaction scale, mmol of 3-methyltetrahydropyran	Yield of **84**/ mol %[c]	Purity[b] %	Appearance
DB1	50	34.6	93.2	Slightly brown oil
DB2	100	29.5	94.6	Slightly brown oil
DB3	100	44.7	99.3	Colourless clear oil

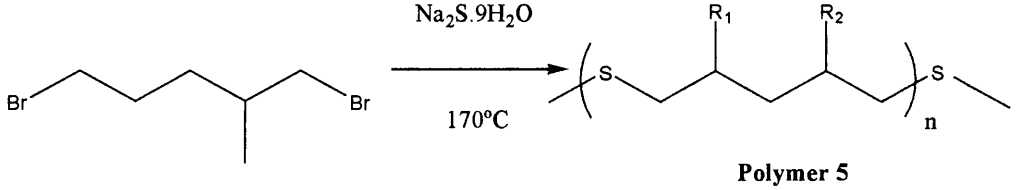
[a] 3-Methyltetrahydropyran (50 mmol) was refluxed for 2 h in the presence of hydrobromic acid (50 mmol) and concentrated sulfuric acid (60 mmol).

[b]As determined by GC.

[c]Isolated by reduced pressure distillation.

3.2.2 Attempted synthesis of Polymer 5 from the Method B reaction of 1,5-dibromo-2-methylpentane

The next step was the polymer forming step. Method B (Scheme 3.3) was first attempted. This method had been successful for producing linear polymers from 1,6-dibromohexane and 1,4-dibromobutane,[12] and therefore it seemed likely that it would proceed for a slightly hindered 1,5-dibromopentane. It can be assumed that the methyl group at the 2 position only introduces a small degree of steric hindrance and therefore would not be expected to directly affect the reactivity of the terminal bromides towards the sodium sulfide nucleophile to any significant extent.



84

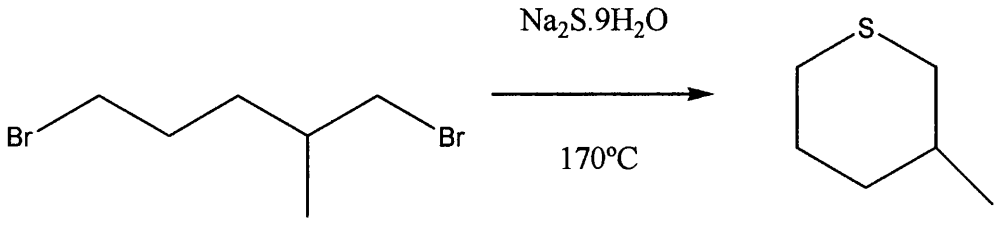
Polymer 5

Where one R=CH_3 and the other = H

Scheme 3.3: The application of Method B polymer forming conditions to 1,5-dibromo-2-methylpentane (**84**).

After work up the resulting crude oil obtained from the reaction had a distinct sulfourous smell and it also weighed approximately half the amount of the original dibromide starting material used. These observations seemed a good indication that

the polymer step had proceeded and that the heavy bromine atoms were lost and replaced by sulfur. The crude oil was subjected to reduced pressure distillation in order to remove any remaining dibromide (**84**) or any other volatile components from the polymeric material that was assumed to be present. Surprisingly, the majority of the crude oil (1.44 g) was isolated by distillation at 70 °C and 20 mmHg of pressure. GC, NMR and MS analysis indicated that the distilled material was in fact 3-methyltetrahydrothiopyran (**85**, Scheme 3.4).



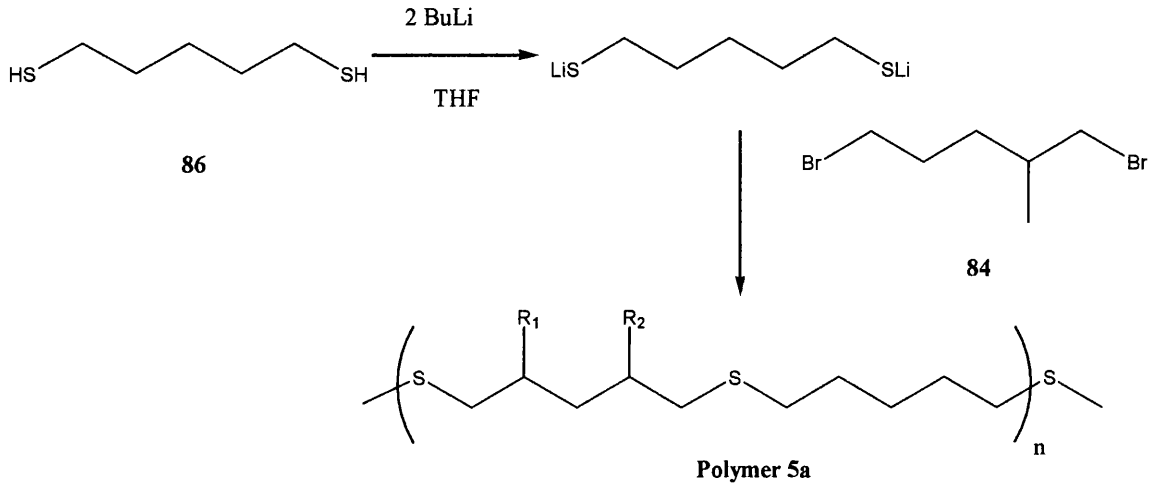
84 **85**

Scheme 3.4: Synthesis of 3-methyltetrahydrothiopyran (**85**) for the reaction of 1,5-dibromo-3-methylpentane (**84**) with sodium sulfide under Method B conditions.

3-Methyltetrahydrothiopyran (**85**) was isolated in a 75 % yield, with a purity of 97.6 % as determined by GC analysis. The reaction of 1,5-dibromo-2-methylpentane (**84**) and sodium sulfide to synthesise 3-methyltetrahydrothiopyran has been reported in the literature.[2] The method used in that case was a reflux in an aqueous/ethanolic solution. Although the conditions used in this polymer forming step are different (solvent free, higher temperature), the cyclic sulfide was obtained in similar yield. The competition between polymerisation and cyclisation will be discussed in Section 3.7.

To avoid the cyclic sulfide formation the alternative polymer forming procedure (Method A) was followed. Of course, the Method A procedure results in the incorporation of two separate spacing groups. One group from the dibromide, and the other from the dithiol. However, the equivalent branched dithiols are not commercially available. The dithiols can be synthesised from the dibromide by the reaction with sodium hydrosulfide (NaSH) or with thiourea.[3] However, these reactions are typically not quantitative. Therefore, for the dibromides the non-quantitative nature of the reaction would predictably lead to even lower yields and result in a mixture of components being present at the end of the reaction which

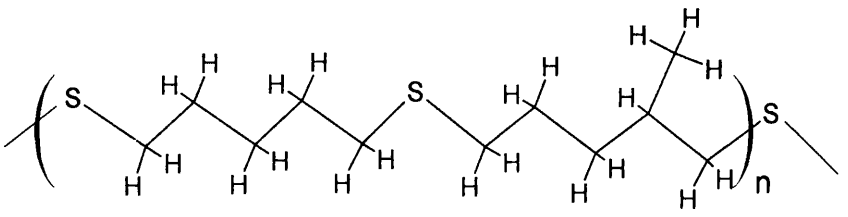
would likely include the starting material and semi-reacted bromothiols. Separating the desired dithiol from this mixture is likely to be difficult considering the closely related physical properties of the predicted components. More notably, the reaction and subsequent tedious separation would be rendered very unpleasant due to the extreme odour associated with the dithiols. In light of this prediction, it was decided that the commercially available linear 1,5-pentanedithiol (**86**) would be used in the Method A procedure and that the subsequent semi-branched polymer (**Polymer 5a**) would be synthesised (Scheme 3.5).



Scheme 3.5: Synthesis of **Polymer 5a** by Method A from 1,5-dibromo-2-methylpentane (**84**) and 1,5-pentanedithiol (**86**).

The polymer step proceeded successfully to give a slightly yellow coloured oil in a 68 % yield. Analogously to the branched polymers synthesised in chapter 2, these polymers exist as oils, presumably for the same reason also stated in chapter 2 (see Section 2.6).

The polymer was characterised by ^{1}HNMR. The interpretation of the ^{1}HNMR spectrum was simplified by assigning the protons into 3 main types that resonate in specific regions of the spectrum (Figure 3.1).



Polymer 5a

Figure 3.1: Illustration of the protons in the repeating unit that are responsible for the three main groups of signals observed in different regions of the ^{1}HNMR spectrum of **Polymer 5a**.

The 3 groups of protons can be categorised as-

1) protons adjacent to sulfur - which resonate at around 2.5 ppm (8 H)

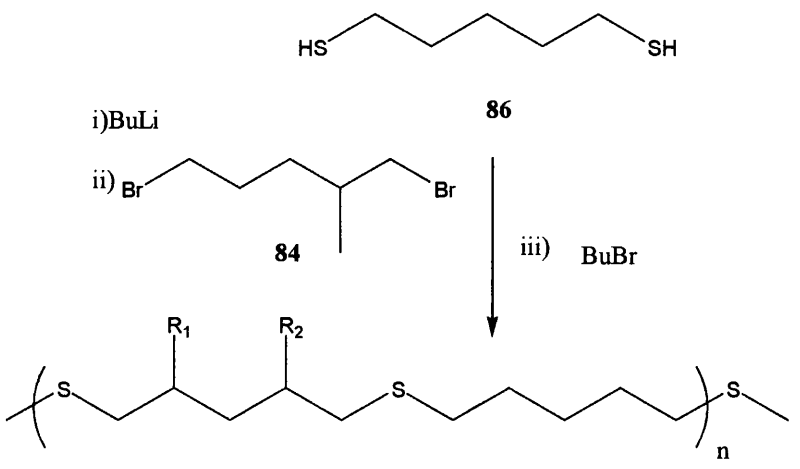
2) protons on the methyl branch - which resonate at around 1 ppm (3H)

3) protons on the alkyl region not adjacent to sulfur - which resonate between 1.2-1.7 ppm (11H).

The theoretical integration is 1:2.66:3.66. The observed integration was 1.00:2.68:3.92.

This simplification contains some inaccuracies due to the presence of a small amount the unreacted bromide group being present. The CH_3 on the terminal bromide chain has been included into proton group 2; the CH_2Br protons that resonate at around 3.5 ppm have been included into proton group 1 and all the remaining protons on the small amount of the unreacted terminal bromide group resonated within the range of proton group 3. Also, the protons on the carbon adjacent to the carbon with the methyl branch are diastereotopic, giving rise to a more complex mixture of proton environments. The simplification is further complicated by the fact that the unreacted bromide (terminal) groups in this case may be present with two separate orientations - ($BrCH_2CH(CH_3)CH_2CH_2CH_2S$-polymer) and ($BrCH_2CH_2CH_2CH(CH_3)CH_2S$-polymer). Despite these complications the theoretical and the observed proton integrations still correlated reasonably well. The M_n of the polymer was determined as 2440 by GPC.

The 1,5-dibromo-2-methylpentane (**84**) polymer reaction with 1,5-pentanedithiolate (**86**) was also carried out with the addition of *n*-bromobutane as a terminal group (Scheme 3.6).

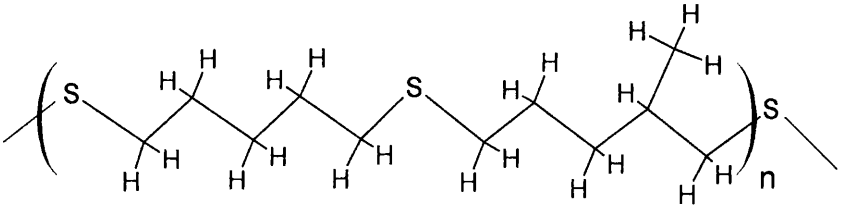


Polymer 5b

Where 1 R = CH_3 and the other = H

Scheme 3.6: Synthesis of **Polymer 5b** by Method A from 1,5-dibromo-2-methylpentane and 1,5-pentanedithiol (**86**) with the use of *n*-bromobutane as a terminating agent.

The reaction proceeded successfully to give a thick yellow coloured oil in a yield of 86 %. Once again ^{1}HNMR analysis was used to confirm the formation of the desired polymer. As would be expected the ^{1}HNMR of this polymer product was essentially identical to that of the previous product and the only difference observed arises from the different nature of the terminal groups. The same simplification used above was conducted on this polymer (Figure 3.2).



Polymer 5b

Figure 3.2 Illustration of the protons in the repeating unit that are responsible for the three main groups of signals observed in different regions in the ^{1}HNMR spectrum of **Polymer 5b**.

As above the 3 groups of protons can be categorised as-

1) protons adjacent to sulfur - which resonate at around 2.5 ppm (8 H)

2) protons on the methyl branch - which resonate at around 1 ppm. (3H)

3) protons on the alkyl region not adjacent to sulfur - which resonate between 1.2-1.7 ppm (11H).

The theoretical integration is 1:2.66:3.66. The observed integration was 1.04:2.42:3.77.

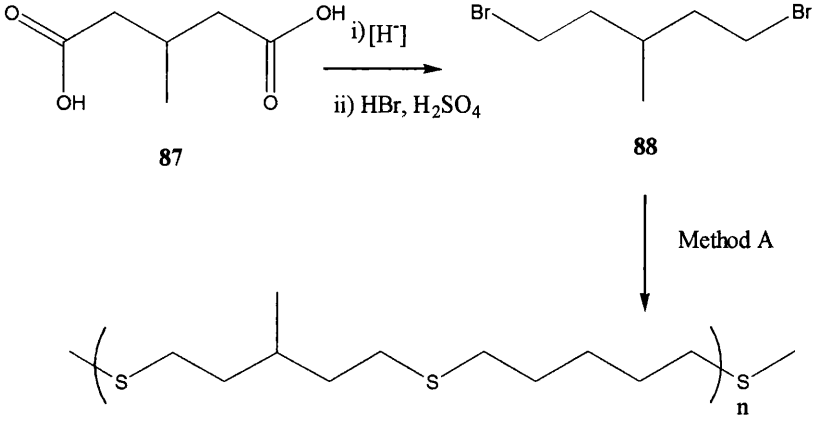
Once again this simplification has some inaccuracies due to the presence of terminal groups. For example the terminal *n*-butyl group ($SCH_2CH_2CH_2CH_3$) gave additional signals which correlate to the above defined colour coded groups, but are present in a different ratio to that in the repeating unit.

The M_n of this polymer was determined as 705 by GPC. This value is considerably lower than the non-terminated polymer (**Polymer 5a**) as would be expected.

In theory one advantage of using the terminating bromobutane agent is that any unreacted thiolate groups should be converted to sulfide groups instead of being worked-up to regenerate the thiol group. This has two main advantages. Firstly the thiol group is not predicted to behave as a catalytic site like the equivalent sulfide (see Section 1.6). Secondly the incorporation of thiol groups into the polymer renders it more odorous and therefore makes it more undesirable for practical reasons. For these reasons all the future polymers synthesised by Method A herein have been carried out with the addition of *n*-bromobutane to create terminal groups.

3.3 Synthesis of branched Polymer 6 from 1,5-dibromo-3-methylpentane.

3-Methylglutaric acid (**87**) is commercially available and can be converted into 1,5-dibromo-3-methylpentane (**88**) by simple functional group interchange as illustrated in Scheme 3.7.

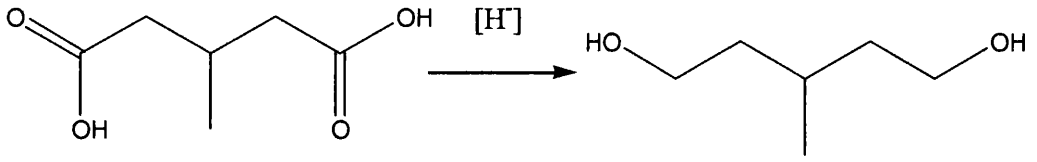


Polymer 6

Scheme 3.7: Synthetic route to **Polymer 6** from the commercially available 3-methylglutaric acid (**87**).

3.3.1 Synthesis of 3-methylpentane-1,5-diol by the reduction of 3-methylglutaric acid.

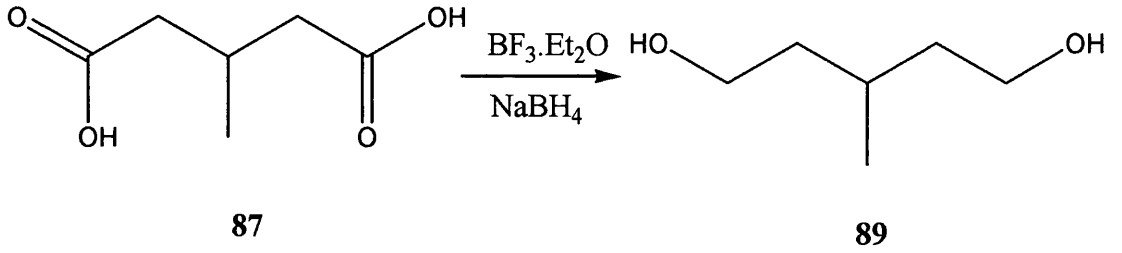
The first step of the synthetic route is the reduction of 3-methylglutaric acid (**87**) to 3-methylpentanediol (**89**) as illustrated in Scheme 3.8.



87 **89**

Scheme 3.8: Reduction of 3-methylglutaric acid (**87**) to 3-methylpentane-1,5-diol (**89**).

Lithium aluminium hydride facilitated reduction[4] was the first reduction step undertaken. The reaction involved stirring the dicarboxylic acid in the presence of 2.5 mole equivalents of $LiAlH_4$ in dry THF for 4 h. As the reaction proceeded it was observed that there was a significant amount of insoluble white material present that seemed to affect the stirring efficiency of the reaction. After simple aqueous work-up it became apparent that the desired product resided in the aqueous phase. The water layer was then removed by rotary evaporation to give a white powder residue. The desired diol (**89**) was then distilled from the residue under reduced pressure to obtain a 38 % yield. The reaction was repeated on a larger scale in order to obtain a sufficient amount of the diol for the remaining synthetic steps and a similar yield of 41 % was obtained. The yields obtained were lower than desired and this was probably due to the poor stirring and/or solvation of the reaction intermediate as observed by the formation of the white precipitate. The proposed synthetic routes to other novel target polymers also involve the initial reduction of a dicarboxylic acid and therefore it was valuable at this stage to investigate the success of other reducing methods. The obvious choice was the diborane facilitated reduction.[5] The method used by Cho[6] was undertaken, which involves the in *situ* generation of diborane by the reaction of boron trifluoride diethyl etherate and sodium borohydride (Scheme 3.9).



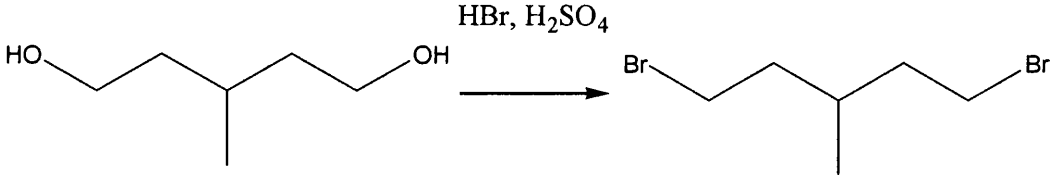
87 **89**

Scheme 3.9: Diborane reduction of 3-methylglutaric acid (**87**) to 3-methylpentane-1,5-diol (**89**).

The reaction involved refluxing the dicarboxylic acid in dry THF in the presence of sodium borohydride and boron trifluoride diethyl etherate for 6 h. This reduction method proceeded much more extensively giving rise to an isolated yield of 93 % of the diol (**89**) after reduced pressure distillation.

3.3.2 Synthesis of 1,5-dibromo-3-methylpentane

For the next stage of the synthetic route 3-methylpentane-1,5-diol (**89**) was treated with HBr and concentrated sulfuric acid to facilitate the substitution to give the required 1,5-dibromo-3-methylpentane (**88**, Scheme 3.10).



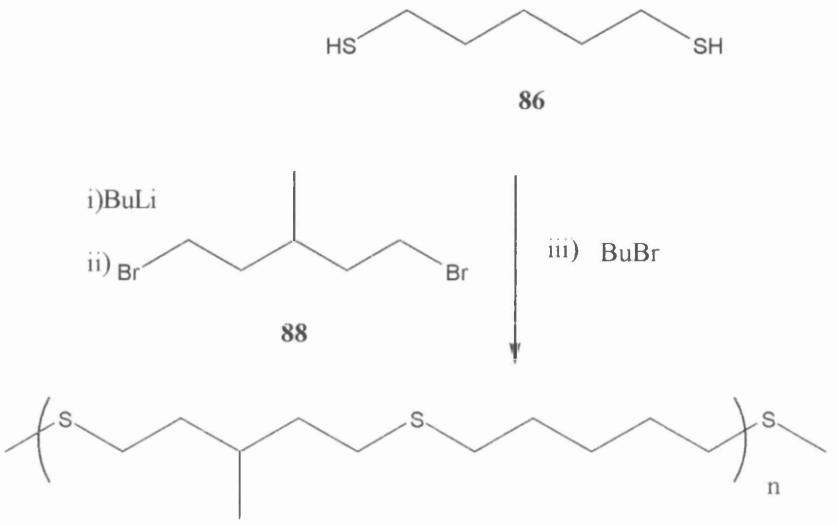
89 **88**

Scheme 3.10: Hydrobromic acid facilitated substitution of 3-methylpentane-1,5-diol (**89**) to give 1,5-dibromo-3-methylpentane (**88**) .

3-Methylpentane-1,5-diol (**89**) was refluxed in the presence of 2 mole equivalents of hydrobromic acid in the presence of excess sulfuric acid for 3 h. Following simple aqueous extractions the crude product was subjected to column chromatography to yield 83 % of the desired dibromide (**88**).

3.3.3 Synthesis of Polymer 6 by the Method A reaction of 1,5-dibromo-3-methylpentane and 1,5-pentanedithiol.

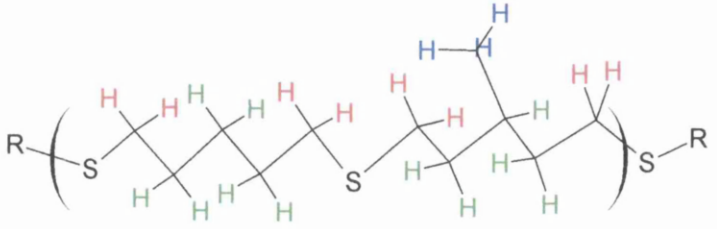
Analogously to the polymer forming step with 1,5-dibromo-2-methylpentane (**84**) described above (see Section 3.2.2) the 1,5-dibromo-3-methylpentane (**88**) was used in the polymer forming reaction conditions of Method A to synthesise **Polymer 6** (Scheme 3.11).



Polymer 6

Scheme 3.11: Synthesis of **Polymer 6** by the Method A reaction of 1,5-dibromo-3-methylpentane (**88**) and 1,5-pentanedithiol (**86**).

Following simple aqueous extractions and the removal of volatile components under reduced pressure a 65 % yield of **Polymer 6** was obtained as a colourless oil. The interpretation of the ^{1}HNMR spectrum was simplified analogously to that of previous polymers. The expected protons were separated into 3 main groups which appear in specific regions of the spectrum (Figure 3.3)



Polymer 6

Figure 3.3: Illustration of the protons in the repeating unit that are responsible for the three main groups of signals observed in different regions of the ^{1}HNMR spectrum of **Polymer 6**.

The 3 groups of protons can be categorised as-

1) protons adjacent to sulfur - which resonate at around 2.5 ppm (8 H)

2) protons on the methyl branch -which resonate at around 1 ppm (3H)

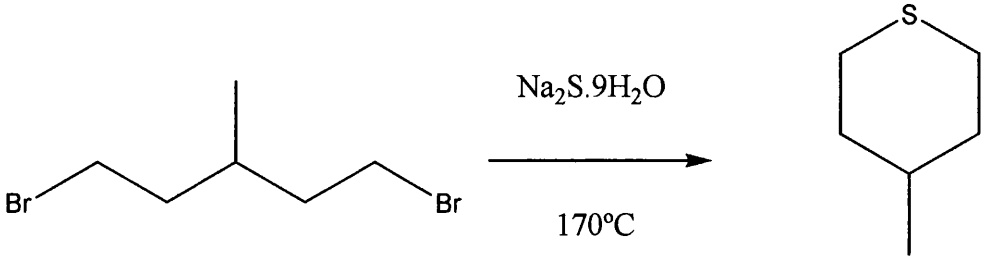
3) protons on the alkyl region not adjacent to sulfur - which resonate between 1.2-1.7 ppm (11H).

The theoretical integration is 1:2.66:3.66. The observed integration was 1:2.42:3.86.

The observed integration matched the predicted integration fairly well, which indicates the successful formation of the desired polymeric material. The same inaccuracies mentioned previously apply to this simplification of the NMR interpretation (see Section 3.2.2). The M_n of the polymer was determined as 2090 by GPC.

3.3.4 Synthesis of 4-methyltetrahydrothiopyran from 1,5-dibromo-3-methylpentane.

The primary objective of this research was the syntheses of novel thiapolymers and the investigation of their potential as selective catalysts for the chlorination of phenols. However, due to the need for the synthesis of a series of methyl-branched 1,5-dibromopentanes the opportunity also arose to synthesise and test a series of cyclic sulfides as potential selective catalysts. Therefore, the Method B conditions were applied to 1,5-dibromo-3-methylpentane (**88**) in order to synthesise 4-methytetrahydrothiopyran (**90**, Scheme 3.12).



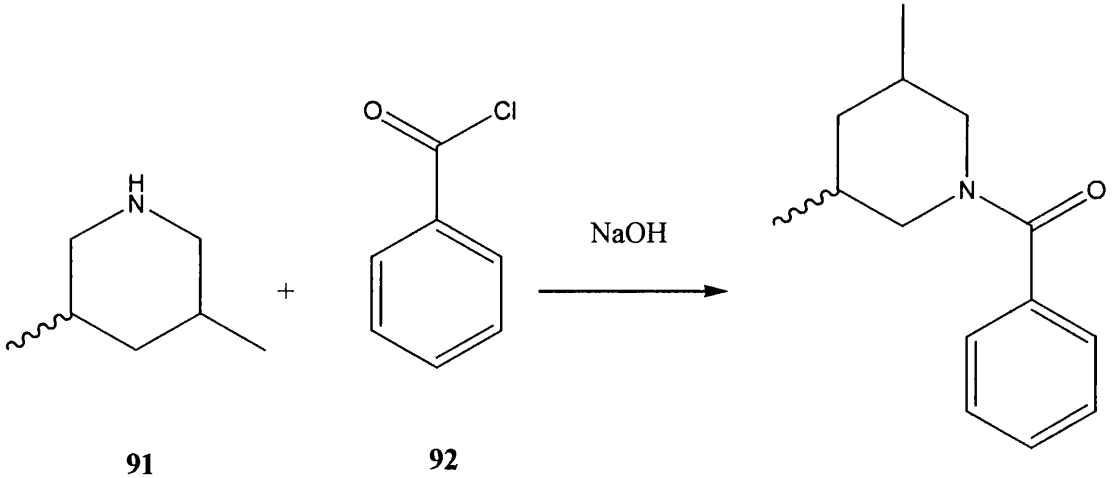
88 **90**

Scheme 3.12: Synthesis of 4-methyltetrahydrothiopyran (**90**) from 1,5-dibromo-3-methylpentane (**88**) under standard Method B conditions.

The reaction proceeded as predicted to yield 79 % of the cyclic product (**90**) after distillation.

3.4 Synthesis of 1,5-dibromo-2,4-dimethylpentane

Analogously to the synthesis of 1,5-dibromo-2-methylpentane (**84**), 1,5-dibromo-2,4-dimethylpentane (**94**, Scheme 3.14) can be synthesized by a nucleophilic ring opening reaction. The 3,5-dimethyltetrahydropyran is not commercially available. However, the equivalent nitrogen analogue 3,5-dimethylpiperidine (**91**) is available. 3,5-Dimethylpiperidine does not undergo simple nucleophilic attack by hydrobromic acid. However, a method known as the von Braun degradation can be undertaken to open up amide derivatives of the piperidine ring.[7] The von Braun reaction involves the initial formation of an amide, which then undergoes degradation when reacted with phosphorous tribromide and bromine to form benzonitrile and a bromide. The first step; the amide formation, was conducted by the reaction of 3,5-dimethylpiperidine with benzoyl chloride (**92**, Scheme 3.13).



91 **92** **93**

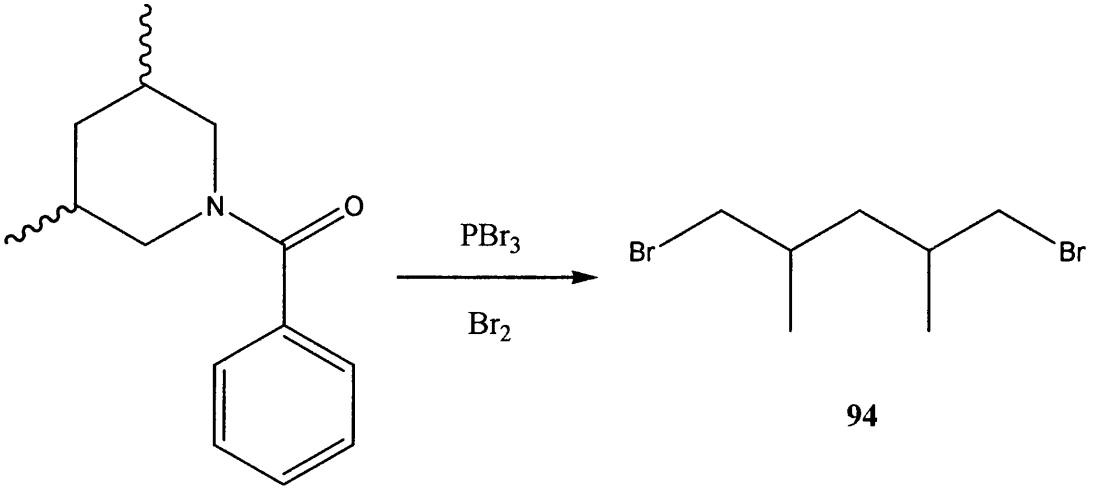
Scheme 3.13: Von Braun step 1; amide (**93**) formation by the reaction of 3,5-dimethylpiperidine (**91**) with benzoyl chloride (**92**).

The piperidine (**91**) was dissolved in an aqueous sodium hydroxide solution and benzoyl chloride was added. A mixture of *cis*- and *trans*-3,5-dimethylpiperidine was used and therefore the product amide (**93**) also existed as a pair of geometric isomers.

Due to the low yield in the next synthetic step (the degradation step) this amide forming step was carried out three times, all in high yields of 93, 94, and 95 %.

3.4.1 Von Braun step 2; amide degredation

The next step, the degradation step was then undertaken. The method used by Nguyen[8] was adapted and followed (Scheme 3.14).



93 **94**

Scheme 3.14: The von Braun amide degradation of amide (**93**) facilitated by phosphorous tribromide and bromine to give 1,5-dibromo-2,4-dimethylpentane (**94**).

A couple of small changes were made to the original procedure; the reaction was conducted in dichloromethane instead of carbon tetrachloride and the crude product was extracted into hexane as opposed to ligroin (mineral oil).

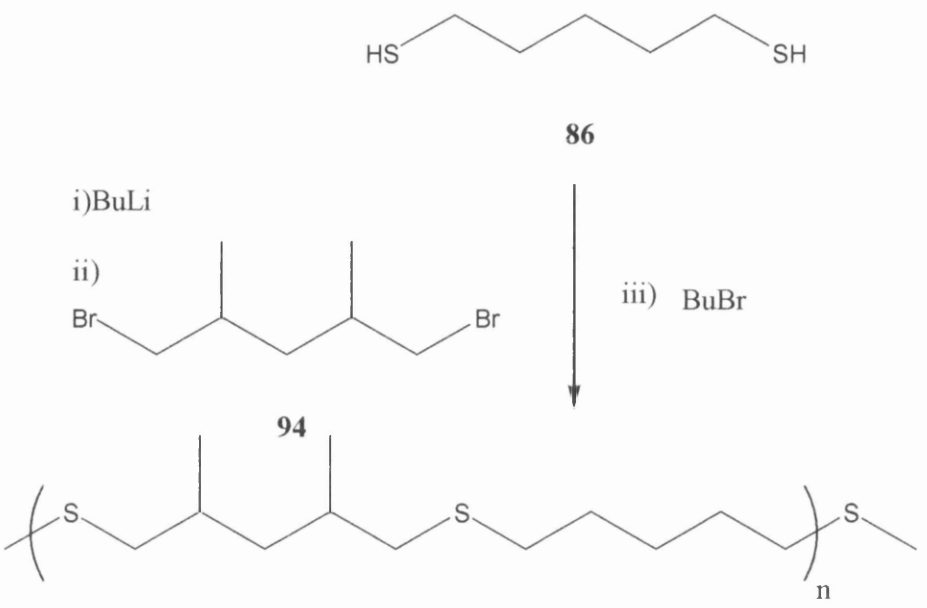
The procedure used was very labour intensive and involved the initial addition of phosphorus tribromide slowly over 2 h and then the addition of bromine slowly over 4 h. This was achieved in sequence using two separate pressure equalising dropping funnels. The liquids were added in incremental amounts approximately every 5-10 minutes. The bromine was then removed by removing the addition funnels and heating the vessel to 90 °C for 2 h. The reaction was then left to stand overnight. The desired bromide together with the expected reaction by-products oxyphosphorus tribromide and benzonitrile were then distilled from the thick black residue. Ice was

then added to decompose the oxyphosphorus tribromide. A series of extraction steps was undertaken, including a washing step with concentrated sulfuric in order to convert the benzonitrile to benzoic acid and any other acidic material. Then a washing step with aqueous sodium carbonate was undertaken in order to remove the benzoic acid. After the extractions the solvents were removed and the crude product was once again distilled under reduced pressure to isolate the desired dibromide. The reaction yielded only 8 % of the desired 1,5-dibromo-2,4-dimethylpentane (**94**). The literature[8] yield was reported as 44 %. The low yield isolated may be due to the modified procedure *e.g.* the dichloromethane may not function as well as the less polar carbon tetrachloride in this reaction.

Due to the low yield an alternative procedure for the von Braun degradation was followed.[9] The alternative method differed from the original because it involved the absence of any solvent and also involved a reflux in hydrobromic acid which was used to convert the benzonitrile to benzoic acid. This alternative procedure gave approximately double the yield of the desired dibromide relative to the original with 18 % product isolated after the second reduced pressure distillation stage. Although this method was not considered satisfactory for eventual synthesis of 1,5-dibromo-2,4-dimethylpentane, it did provide sufficient material for attempted polymer formation and therefore was not studied further.

3.4.2 Polymer forming step from 1,5-dibromo-2,4-dimethylpentane.

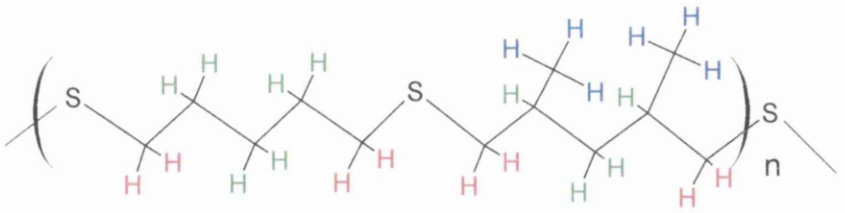
In the same manner to the synthesis of **Polymers 5b** and **6**, the dibromopentane was reacted with 1,5-pentanedithiol (**86**) under standard Method A polymer forming conditions to give **Polymer 7** (Scheme 3.15).



Polymer 7

Scheme 3.15: Synthesis of **Polymer 7** by the Method A reaction of 1,5-dibromo-2,4-dimethylpentane (**94**) and 1,5-pentanedithiol (**86**).

Once again the interpretation of the spectra was conducted by assigning certain groups of protons into three distinct groups (Figure 3.4).



Polymer 7

Figure 3.4: Illustration of the protons in the repeating unit that are responsible for the three main groups of signals observed in different regions of the ^{1}HNMR spectrum of **Polymer 7**.

The reaction proceeded successfully to yield 56 % of a thick clear colourless oil obtained after simple aqueous extractions and drying in a vacuum oven.

As illustrated above the three main groups of protons can be characterised as-

1) protons adjacent to sulfur - which resonate at around 2.5 ppm (8 H)

2) protons on the methyl branches - which resonate at around 1 ppm (6H)

3) protons on the alkyl region not adjacent to sulfur - which resonate between 1.2-1.7 ppm (10H).

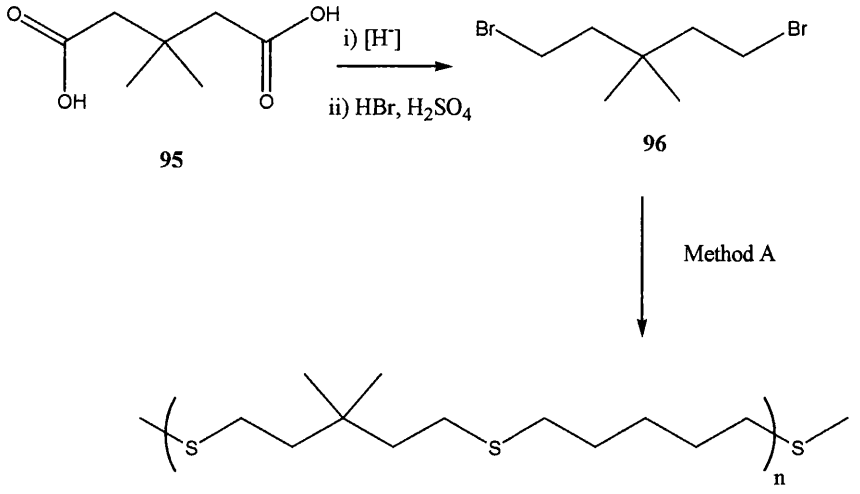
The theoretical integration is 1: 1.33 : 1.66. Observed integration was 1: 1.34 : 1.70

Once again the theoretical and the observed integrations correlate well, which indicates the correct formation of the polymer. The M_n of the polymer was determined as 1320 by GPC.

Due to the low amount of 1,5-dibromo-2,4-dimethylpentane (**94**) obtained and the low yield in the employed synthetic route no attempt has been made to synthesise 3,5-dimethyltetrahydrothiopyran.

3.5 Proposed synthetic route to Polymer 8 from 1,5-dibromo-3,3-dimethylpentane.

A synthetic route analogous to that conducted for the synthesis of **Polymer 6** from 3-methylglutaric acid (see Section 3.3.3) was proposed for the synthesis of **Polymer 8** from 3,3-dimethylglutaric acid (**95**, Scheme 3.16).



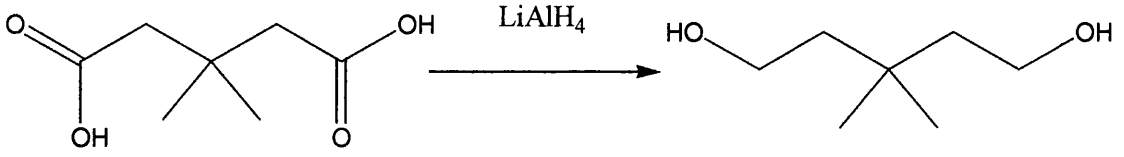
95 **96** **Polymer 8**

Scheme 3.16 Synthetic route to **Polymer 8** from 3,3-dimethylglutaric acid (**95**) *via* 1,5-dibromo-3,3-dimethylpentane (**96**).

3.5.1 Reduction of 3,3-dimethylglutaric acid.

The reduction of 3-methylglutaric acid (**87**, see Section 3.3.1) was conducted previously by two methods- firstly by lithium aluminium hydride and secondly by diborane. A large disparity in the success of these methods was observed with the latter giving quantitative yields and the former giving yields of around 40 %.

However, for monocarboxylic acids both methods have been reported to proceed in high to quantitative yields.[4,5] In the first instance, the reduction of 3,3-dimethylglutaric acid (**95**) was carried out using the lithium aluminium method (Scheme 3.17) in order to further assess the application of this method for the reduction of dicarboxylic acids.

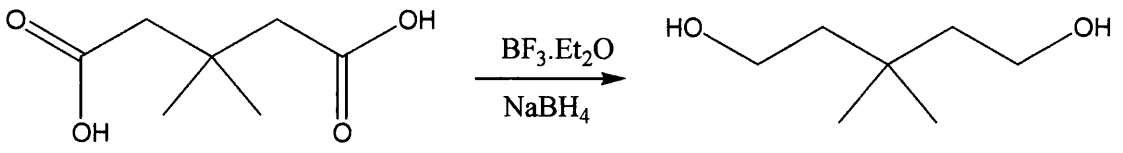


95 **97**

Scheme 3.17: Reduction of 3,3-dimethylglutaric acid (**95**) by lithium aluminium hydride to form 3,3-dimethyl-1,5-pentanediol (**97**).

The method employed was the same as that used for the synthesis of 3-methyl-1,5-pentanediol (**89**, see Section 3.3.1). The first reaction was conducted using 10 mmol of 3,3-dimethylglutaric acid (**95**) and the second was carried out on a larger scale using 20 mmol of 3,3-dimethylglutaric acid in order to obtain more product material for subsequent synthetic steps. The yields of these reactions were 51 and 38 % respectively, which are comparable to the yields obtained for the reduction of 3-methylglutaric acid (**87**). In both cases a white precipitate was generated during the reaction which appeared to significantly hinder the stirring efficiency of the reactions. In an attempt to prevent the formation of the precipitate and to push the reaction to completion the reduction was repeated but was refluxed for 12 h (as opposed to stirring for 4 h at ambient temperature) with the use of 20 % more dry THF. In this reaction the persistent white precipitate appeared after approximately 2 h of reflux. However, the amount of the precipitate did not appear to be as great as in previous reactions and the stirring efficiency did not appear to have been reduced to any significant extent. Not surprisingly, this reaction gave the best yield of 64 %. The change in conditions, such as increased temperature, solvation and stirring efficiency as well as an increased reaction time had a favourable effect on the reaction. It is conceivable that by using even more solvent (dry THF) then the solvation and therefore also the stirring efficiency could be further enhanced, pushing the reaction

even further to completion. However, that has not been conducted here. Instead, the alternative diborane reduction was carried out preferentially (Scheme 3.18).



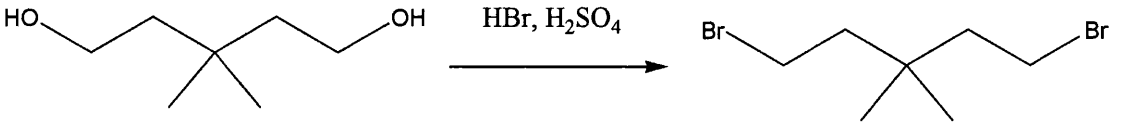
95 **97**

Scheme 3.18: Reduction of 3,3-dimethylglutaric (**95**) acid facilitated by diborane to form 3,3-dimethyl-1,5-pentanediol (**97**).

The procedure used for the reduction of 3-methylglutaric acid (**87**, see Section 3.3.1) was repeated for 3,3-dimethylglutaric acid (**95**). This diborane facilitated reduction once again proceeded in a quantitative fashion, with an isolated yield of diol (**97**) of 97 % after reduced pressure distillation. Following the brief investigation of both of these methods for the reduction of dicarboxylic acids it can be concluded that the lithium aluminium hydride method is persistently hindered by the generation of a precipitate which ultimately leads to a lower yield of the diol. The diborane method proceeded quantitatively and for this reason was used exclusively for the reduction of dicarboxylic acids for the remainder of work reported here.

3.5.2 Synthesis of 1,5-dibromo-3,3-dimethylpentane.

The next step of the synthesis was simple hydrobromic acid facilitated substitution to give 1,5-dibromo-3,3-dimethylpentane (**96**) analogously to that used to synthesise 1,5-dibromo-3-methylpentane (**88**, see Section 3.3.2). The same method was applied to 3,3-dimethyl-1,5-pentanediol (**97**, Scheme 3.19).



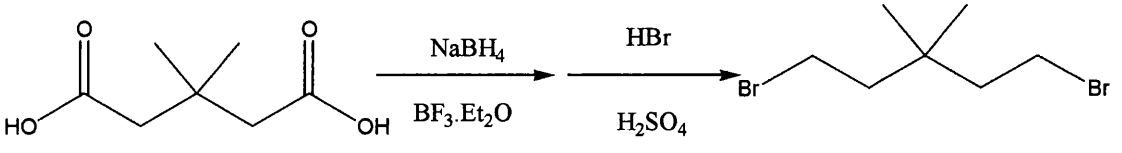
97 **96**

Scheme 3.19: Substitution of 3-methylpentane-1,5-diol (**97**) to give 1,5-dibromo-3,3-dimethylpentane (**96**) facilitated by hydrobromic acid.

The substitution was successful in forming the desired dibromopentane but the isolated yields were low. Two reactions were carried out and after aqueous workup followed by reduced pressure distillation gave rise to poor yields of the dibromide (**96**) of 41 and 43 %. These yields were lower than expected, and also represented approximately half the yield of that reported in a similar substitution in Section 3.3.2. TLC analysis of the crude product indicated that all of the starting material had been consumed and therefore the low yields were not the result of an incomplete reaction. All the aqueous phases were re-extracted with DCM in an attempt to recover the lost organic material, but only a negligible amount of material was obtained. It is conceivable that the loss of material may be the result of degradation facilitated by the harsh reaction conditions of concentrated sulfuric acid and HBr. If this is true then it is likely that a higher yield could be obtained if this substitution was conducted in the absence of the sulfuric acid. However, this has not been conducted here.

3.5.3 Synthesis of 1,5-dibromo-2,4-dimethylpentane by a sequential reduction-substitution procedure.

In order to obtain enough 1,5-dibromo-3,3-dimethylpentane (**96**) to synthesise a sufficient amount of **Polymer 8** and 4,4-dimethyltetrahydrothiopyran (**98**, Scheme 3.22) more synthetic reactions were carried out. As reported the reduction step facilitated by the in *situ* generation of diborane proceeded quantitatively. This prompted an investigation into the possibility of carrying out the substitution on the crude reduction product prior to any attempt to isolate the diol (**96**, Scheme 3.20).



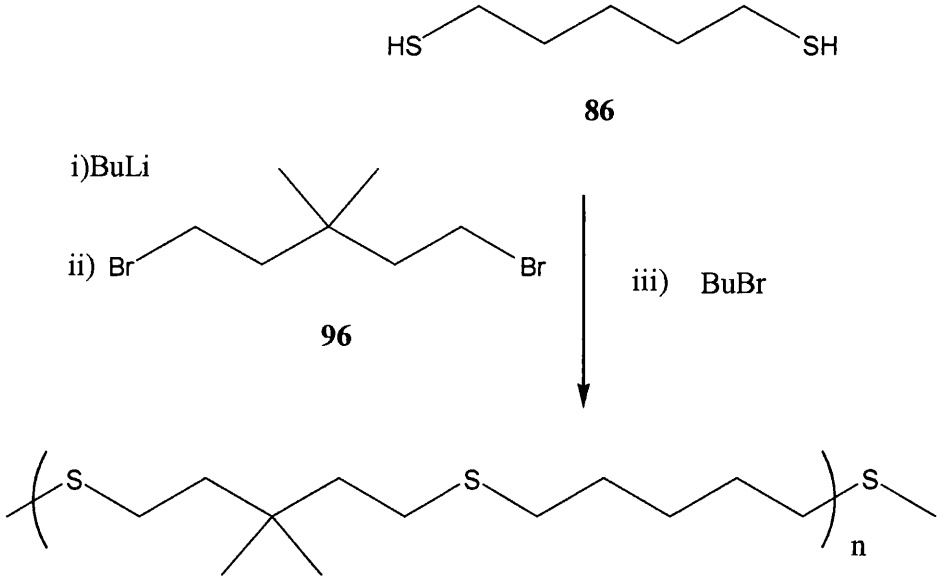
95 **96**

Scheme 3.20: Sequential reduction-substitution of 3,3-dimethylglutaric acid (**95**) to synthesise 1,5-dibromo-3,3-dimethylpentane (**96**).

The reduction step was carried out as before (see Section 3.5.1) and was then quenched with water. The solvents (including water) were then removed by rotary evaporation to give the crude material presumed to contain the diol (**97**). Two mole equivalents of hydrobromic acid and 4 mole equivalents of concentrated sulfuric acid were then added to this crude product. It was considered that there was a possibility that the hydrobromic acid/sulfuric acid mixture may react with some of the inorganic material present in the crude reduction product causing complications in the reaction. However, the substitution conditions used previously (see Section 3.5.3) were applied to the crude material and following work-up by simple aqueous extraction and then column chromatography a yield of 63 % of 1,5-dibromo-3,3-dimethylpentane (**96**) was obtained.

3.5.4 Synthesis of Polymer 8 from 1,5-dibromo-3,3-dimethylpentane.

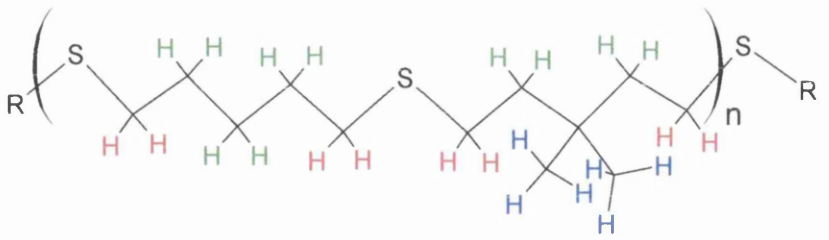
The 1,5-dibromo-3,3-dimethylpentane (**96**) was then used in the polymer forming Method A reaction and was reacted with 1,5-pentanedithiolate (**86**, Scheme 3.26).



Polymer 8

Scheme 3.21: Synthesis of **Polymer 8** by the Method A reaction of 1,5-dibromo-3,3-dimethylpentane (**96**) and 1,5-pentanedithiol (**86**).

The crude product was isolated and was analysed by ^{1}HNMR. The comparison to the expected signals was once again performed (Figure 3.5).



Polymer 8

Figure 3.5: Illustration of the protons in the repeating unit that are responsible for the three main groups of signals observed in different regions of the ^{1}HNMR spectrum of **Polymer 8**.

As illustrated above the three main groups of protons can be characterised as-

1) protons adjacent to sulfur - which resonate at around 2.5 ppm (8 H)

2) protons on the methyl branches - which resonate at around 1 ppm (6H)

3) protons on the alkyl region not adjacent to sulfur - which resonate between 1.2-1.7 ppm (10H).

The theoretical integration is 1:1.33:1.66. The observed integration was 1:1.69:2.47.

The observed ^{1}HNMR integrals did not match the theoretical very well. Therefore, it can be concluded that the crude product was not the desired polymeric material. The integration showed that there appeared to be a relative excess of alkyl protons not adjacent to sulfur. The protons adjacent to sulfur gave rise to 3 peaks, one of which was a triplet that resonated at 2.64 ppm which is further downfield than it would be expected for the desired sulfide and may be from methylene protons adjacent to thiol groups. It was originally speculated that these observation could be explained by the presence of remaining dithiol starting material. This considered, the residue was dissolved in DCM (2 mL) and the oily material was re-precipitated by the addition of methanol (20 mL). The small amount of insoluble heavy oil was carefully separated by a separating funnel. The oil was then heated to 130 °C at 2mmHg for 4 h to remove any remaining 1,5-pentanedithiol (**86**). The resulting residue was sent for ^{1}HNMR analysis. The ^{1}HNMR was essentially identical to that obtained for the original crude product.

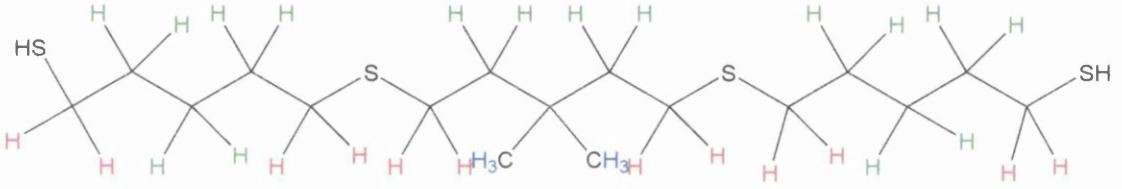
The residue was clearly not the desired polymer and also did not contain any remaining starting material or remaining bromide groups. At this stage the reaction was repeated and a very similar result was obtained, excluding the possibility of an anomaly in the previous reaction. The high integration of the groups present at

2.64 ppm suggests that a thiol rich material may have formed. The observed proton integration corresponds quite well to a hypothetical oligomer, **Oligomer 1** (Figure 3.6).

Oligomer 1

Figure 3.6: Hypothetical oligomer compound (**Oligomer 1**).

The theoretical integration for **Oligomer 1** is 1:2:2.6. The observed integration was 1:1.69:2.47.



Oligomer 1

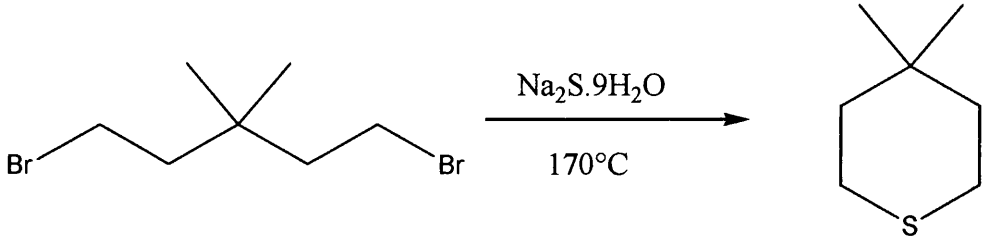
Figure 3.7: Illustrations of the 3 main types of protons on **Oligomer 1** that appear in the previously defined groups that occupy certain regions of the ^{1}HNMR spectrum.

The NMR indicates the formation of oligomers and it is likely that the hypothetical **Oligomer 1** is the dominant species of the mixture due to the good correlation between the theoretical and observed NMR signals. This observation suggests that the propagation stage of polymer formation did not proceed effectively. Assuming that the suggested oligomer is indeed the major component then it can be further speculated that the 1,5-dibromo-3,3-dimethylpentane (**96**) reacts well with 2 equivalents of 1,5-pentanedithiolate (**86**) to form **Oligomer 1**. If so, this would consume all the available dithiolate and more than half of the dibromoalkane. The next step (propagation) would involve the reaction of the oligomeric dithiolate and the dibromoalkane. The NMR indicates a relatively low amount of sulfide has formed suggesting that propagation does not proceed much beyond this initial stage, indicating that the reaction of the remaining 1,5-dibromo-3,3-dimethylpentane and the oligomeric dithiolates was much less feasible than the original 1,5-pentanedithiolate.

This could be understood in terms of the relatively lower mobility in solution of the oligomer and the fact that when it is formed the concentration of the electrophilic species (dibromoalkane) is inevitably reduced (by up to more than half). Any remaining dibromoalkane would have been lost in the 'drying' of the polymer in the vacuum oven. Not surprisingly, the GPC indicated a low molecular weight species and gave retention times persistently beyond the range of the calibration graph. The oligomeric mixture isolated from this reaction was also tested as a catalyst for the chlorination of phenols.

3.5.5 Synthesis of 4,4-dimethyltetrahydrothiopyran.

1,5-Dibromo-3,3-dimethylpentane (**96**) was then reacted with sodium sulfide under the standard Method B conditions with the intention of synthesising 4,4-dimethyltetrahydrothiopyran (**98**, Scheme 3.22).



96 **98**

Scheme 3.22: Synthesis of 4,4-dimethyltetrahydrothiopyran (**98**) from 1,5-dibromo-3,3-dimethylpentane (**96**) under the standard Method B conditions.

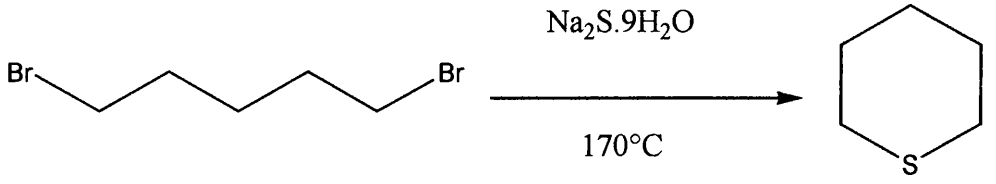
The standard Method B conditions were applied to 1,5-dibromo-3,3-dimethylpenatane (**96**) and the cyclic product (**98**) was isolated by distillation in a yield of 58 %. Incidentally, there was also some starting material isolated from this reaction which was not observed when the other tetrahydrothiopyrans were synthesised by Method B. This is further indirect evidence that the methyl groups present in this substrate (**96**) reduce the reactivity of the terminal bromide groups towards nucleophiles.

3.6 Synthesis of some linear polythiaalkanes containing pentylene groups in the repeating unit.

As previously mentioned, no linear pentylene containing polythiaalkanes had previously been synthesised. It was deemed desirable to synthesis some novel linear polythiaalkanes in order to make direct comparisons to the branched analogues synthesised herein. The linear Polymer 5-5 was chosen due to it being the direct linear analogue to all the branched polymers synthesised in this chapter.

3.6.1 Attempted Synthesis of Polymer 5-5.

The first polymer forming process carried out in an attempt to synthesise Polymer 5-5 was the Method B reaction of 1,5-dibromopentane (**99**). However, it was carried out with the expectation of actually obtaining the cyclic tetrahydrothiopyran product (**100**, Scheme 3.23).



99 **100**

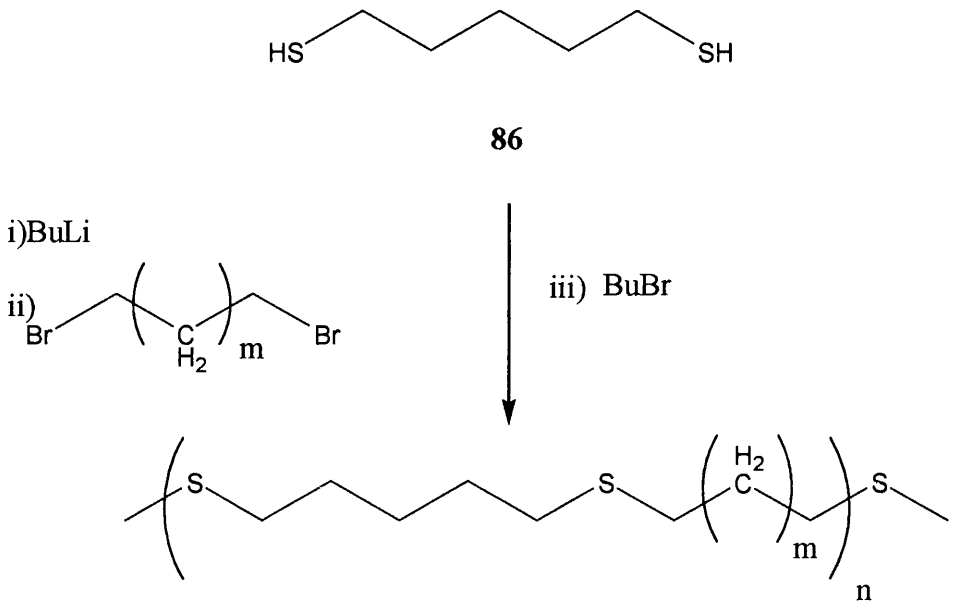
Scheme 3.23: Synthesis of tetrahydrothiopyran (**100**) by Method B from 1,5-dibromopentane (**99**).

The reaction proceeded as predicted to give an isolated yield of 42 % of the cyclic product (**100**) after distillation. No starting material (**99**) or polymeric material was observed and it is likely that the organic material unaccounted for was due to the evaporation of the volatile cyclic product, probably lost during isolation by distillation. A better yield could probably be obtained if the distillation was conduced with the use of liquid nitrogen as a coolant as opposed to a water condenser.

3.6.2 The syntheses of other novel linear pentylene containing thiapolymers.

Method A was then used in order to synthesise Polymer 5-5 and some other pentylene containing linear thiapolymers. 1,5-Pentanedithiolate (**86**) was reacted with

1,5-dibromopentane, 1,4-dibromobutane, 1,3-dibromopropane and 1,6-dibromohexane in order to synthesise Polymers 5-5, 5-4, 5-3, and 5-6 (Scheme 3.24).



Where m= 1,2,3,4

Scheme 3.24: Syntheses of novel linear Polymers 5-3 (m=1), 5-4 (m=2), 5-5 (m=3) and 5-6 (m=4) from the Method B reaction of 1,5-pentanedithiol (**86**) and a series of linear dibromoalkanes.

The reactions all proceeded successfully to yield the expected polymers as white powders. The yields and the M_n values of the obtained polymers are shown in Table 3.2.

Table 3.2: The results of the polymer forming reactions according to Scheme 3.24.

m[a]	Polymer	Yield/ mol %	M_n
1	5-3	78	7250
2	5-4	79	6390
3	5-5	77	6160
4	5-6	65	6840

[a]See Scheme 3.24.

All the reactions proceeded in moderate yields (65-79) and resulted in relatively large molecular weight materials (M_n = 6260-7250).

3.7 Competition between polymerisation and cyclisation

The competition between the intra- and inter- molecular reactions is a common consideration in the field of polymer synthesis. The competition is governed by two main factors: firstly, the likelihood for the two reactive groups to come together (entropy factor), which becomes less likely as the chain length gets bigger[10] and therefore assuming the functional groups are on opposite terminal ends, then the longer the monomer the more chance of the reaction occurring intermolecularly; secondly the thermodynamic factor (enthalpy), which is strongly dependent on the size of the ring formed. Table 3.3[11] shows the heat of combustion values for some cycloalkanes.

Table 3.3: Heats of combustion values of cycloalkanes (C3-C9).[11]

Size of ring	**Heat of combustion per CH_2, kcal/mol**
3	166.3
4	163.9
5	158.7
6	157.4
7	158.3
8	158.6
9	158.8

The larger rings are more thermodynamically stable as they can exist in conformations which exhibit less strain. Carboxylic rings smaller than 6 member rings possess increasing amounts of strain. However, it must be noted that the presence of a sulfur atom in the ring, resulting in longer C-S bonds and narrower C-S-C bond angles, will change the figures somewhat.

For the reaction of 1,5-dibromopentanes with sodium sulfide it is clear that both the enthalpy and entropy factors are in favour of cyclisation *i.e* the two ends are likely to interact and then form the relatively thermodynamically stable 6 member ring. Therefore, it is not surprising that when this reaction was conducted, tetrahydrothiopyran was obtained exclusively. Conversely, when 1,4-dibromobutane and 1,6-dibromohexane were reacted with sodium sulfide under the standard

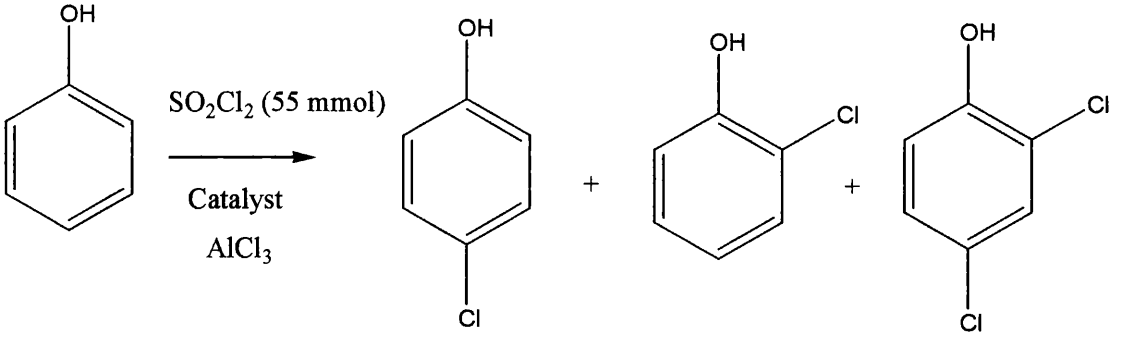
Method B conditions then the polymeric sulfides were produced.[12] As we move from 1,5-dibromopentane to 1,6-dibromohexane then both the enthalpy and entropy factors are likely to become less favourable for cyclisation. For 1,4-dibromobutane it is highly conceivable that the reactive groups are likely to interact and therefore it is the enthalpy factor, the relatively low thermodynamic stability of the 5 member sulfur containing ring, which results in the competition being in favour of polymerisation. It is noteworthy to mention that it is also conceivable that the 5 member ring does form but its relatively low stability may make it susceptible to subsequent ring opening reactions facilitated by the nucleophilic species present, which would ultimately lead to polymer formation.

Relative to the 1,5-dibromopentane the methyl substituted 1,5-dibromopentanes synthesized in this chapter are actually more likely to exist in conformations that result in interaction between the terminal ends. In other words, they are predicted to have lower entropy factors making cycilisation even more feasible.

3.8 Chlorination results using the novel branched polythiaalkanes and tetrahydrothiopyrans derived from various 1,5-dibromopentanes as catalysts.

The polymeric sulfide materials and the cyclic sulfide materials synthesised in this chapter were tested as potential selective catalysts for the chlorination of phenols. The chlorination of phenol was studied first (Scheme 3.25).

3.8.1 Chlorination of phenol; baseline results.



P (50 mmol) **PCP** **OCP** **DCP**

Scheme 3.25: The chlorination of phenol.

The baseline results for the chlorination of phenol in the absence of a sulfide catalyst reported in Section 2.8.2 are recorded again in Table 3.4 for ease of reference.

Table 3.4: Baseline results for the reaction of phenol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	P/ mol %[b]	OCP/ mol %[b]	PCP/ mol %[b]	2,4-DCP/ mol %[b]	*p:o* ratio	Mass balance
-	8.2	21.1	63.7	0.7	3.0	93.7
$AlCl_3$	10.7	17.1	70.1	1.0	4.1	98.9

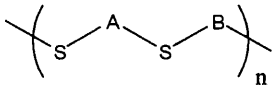
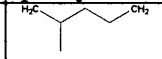
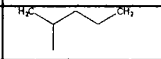
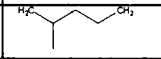
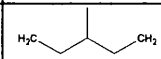
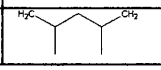
[a] Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (0.375 mmol). For more details see Section 2.15.2.

[b] See Scheme 3.25

3.8.1.1 Chlorination of phenol using some novel branched polymers as catalysts with comparison to their linear analogues.

Using the standard conditions for phenol described in Section 2.15.2 the chlorination was conducted in the presence of the branched polymers synthesised from the methyl substituted 1,5-dibromopentanes as reported in this chapter. The reaction was also conducted using the linear Polymer 5-5 analogue and the crude oligomeric mixture reported in Section 3.5.4. The results are shown in Table 3.5.

Table 3.5: Chlorination of phenol using some novel branched polymers as catalysts with comparison to their linear direct linear analogue.[a]

Catalyst  [Polymer number]		P/ mol %[b]	OCP/ mol %[b]	2,4-DCP/ mol %[b]	PCP/ mol %[b]	*p:o* ratio	Mass balance
A=	**B=**						
pentylene	pentylene	0.6	10.8	1.0	86.5	8.0	98.9
pentylene	 [5a]	8.9	8.3	1.1	78.3	9.4	96.6
pentylene[c]	 [5b]	5.0	6.7	0.0	83.2	12.4	94.9
pentylene[d]	 [5b]	0.7	7.8	4.0	84.3	10.8	96.8
pentylene	 [6]	0.0	9.1	3.0	86.3	9.5	98.4
pentylene	 [7]	0.0	13.1	1.7	83.7	6.4	98.5
Oligomer 1		0.0	13.6	4.4	79.3	5.8	97.3

[a] Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.2.

[b] See Scheme 3.25.

[c] Contains *n*-butyl terminal groups

[d] Repeat of the reaction in the above row.

It is clear that in the presence of these branched polymers there are enhancements in the *para* selectivities with all the result giving a *p:o* ratios in excess of the 4.1 obtained in the baseline experiment. Furthermore, in general, these catalysed reactions tend to go closer to completion with 5 out of the 7 experiments resulting in less than 1 % remaining starting material left at the end of the reaction.

The linear Polymer 5-5 gave a *p:o* ratio of 8.0. All the single methyl branched polymers (**Polymers 5a**, **5b** and **6**) gave marginally higher selctivities. **Polymer 5b** was the most selective and out-performed **Polymer 5a** (no terminal groups) in terms of *para* selectivity as expected (see Section 3.2.2).

The reaction in the presence of **Polymer 5b** was repeated to ascertain how reproducible these chlorination reactions are. This was conducted due to the high potential for variation that exists as a result of certain inconsistencies in the experimentation that have already been highlighted (see Section 2.15.3). The repeated reaction proceeded with a similar *p:o* ratio. However, in the repeated reaction there was a significant amount of **DCP** formed, which was probably because some addition of sulfuryl chloride occurred when the reaction mixture had solidified and therefore when some substrate was exposed to excess chlorinating agent some was also isolated from it. This could have resulted in the observed result were about 4 % **DCP** formed and almost 8 % of the phenol starting material remained. The **Oligomer 1** and **Polymer 7** gave *p:o* ratios of 6.4 and 5.8 respectively which are only marginally better than the baseline results. These low selectivity ratios also show that these catalysts are actually less selective than the linear 5-5 reference catalyst under these conditions.

The remaining novel linear polythiaalkanes synthesised in this chapter were also tested as catalysts for the chlorination of phenol and the results are shown in Table 3.6.

Table 3.6: The chlorination of phenol with sulfuryl chloride in the presence of some novel linear polythiaalkanes.[a]

Catalyst	P/ mol %[b]	OCP/ mol %[b]	PCP/ mol %[b]	2,4-DCP/ mol %[b]	*p:o* ratio	Mass balance
5,6	1.1	9.7	86.3	0.8	8.9	97.9
5,4	3.0	15.7	80.4	1.0	5.1	100.1
5,3	0.0	12.1	83.2	1.0	6.9	96.3

[a]Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.2.

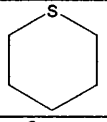
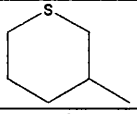
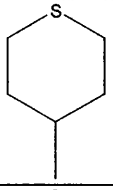
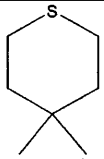
[b] See Scheme 3.25.

Table 3.6 shows that these novel linear polymers gave rise to mild to moderate enhancements in selectivity (1.5-2 times more selective than the baseline) but appear to be marginally less selective than the majority of the branched polymers used (as shown in Table 3.5).

3.8.1.2 Chlorination of phenol using tetrahydrothiopyrans as catalysts.

The cyclic sulfides formed in this chapter were also used and tested as potential selective catalysts for the chlorination of phenols. The majority were freshly prepared and purified by distillation prior to starting the testing phase. The standard conditions derived for the polymers were also applied to these tetrahydrothiopyrans. The results for the chlorination of phenol in the presence of some tetrahydrothiopyrans are shown in Table 3.7.

Table 3.7: Chlorination of phenol using various tetrahydrothiopyrans as catalysts.[a]

Catalyst	P/ mol %[b]	OCP/ mol %[b]	PCP/ mol %[b]	2,4-DCP/ mol %[b]	*p:o* ratio	Mass balance
	5.8	5.0	89.0	0.0	17.8	99.8
	10.8	5.6	83.2	0.0	14.9	99.6
	2.3	6.9	88.1	0.0	12.8	97.3
	6.7	4.8	87.8	0.0	18.3	99.3

[a]Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a cyclic sulfide (0.284 mmol). For more details see Section 2.15.2.

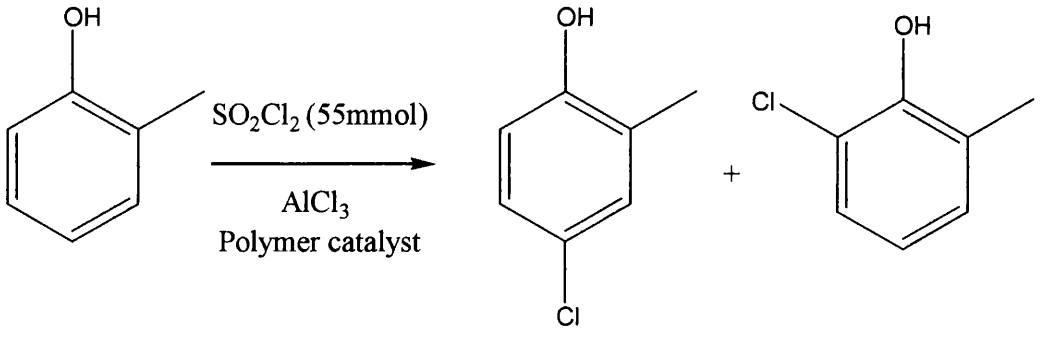
[b] See Scheme 3.25.

It is clear that these cyclic compounds act as better, more selective catalysts for the chlorination of phenol compared to the polymeric materials tested so far under

these conditions. Selectivities in excess of a 4 fold increase on the baseline results can be obtained in the presence of tetrahydrothiopyran and 4,4-dimethyltetrahydrothiopyran. Moreover, it is apparent that if the reactions were forced to completion and 100 % of material was accounted for it would seem feasible to synthesise 90 % or more of the desired *para* chlorinated product in all cases, which is considerably greater than the 70 % **PCP** (with 10 % remaining starting material) observed under the baseline conditions.

3.8.2 The chlorination of *o*-cresol.

The polymeric sulfide materials and the cyclic sulfide materials synthesised in this chapter were next tested as potential selective catalysts for the chlorination of *o*-cresol (Scheme 3.36).



OC (50mmol) **PCOC** **OCOC**

Scheme 3.26: The chlorination of *o*-cresol.

The baseline results for the chlorination of *o*-cresol in the absence of a sulfide catalyst reported in Section 2.15.4 are recorded again in Table 3.8 for ease of reference.

Table 3.8: Baseline results for the chlorination of *o*-cresol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Catalyst	$AlCl_3$ (g)	OC mol%[b]	OCOC mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
—	—	2.0	15.4	78.2	5.1	95.6
—	0.05	9.6	11.9	75.1	6.3	96.6

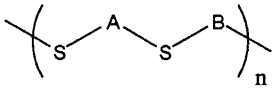
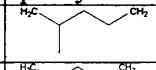
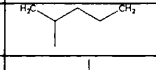
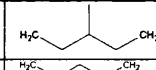
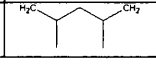
[a] Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (0.375 mmol). For more details see Section 2.15.4.

[b] See Scheme 3.26.

3.8.2.1 Chlorination of *o*-cresol using some novel branched polythiaalkanes as catalysts with comparison to their linear analogues.

Using the standard conditions for *o*-cresol described in Section 2.15.4 the chlorination was conducted in the presence of the branched polymers synthesised from the methyl substituted 1,5-dibromopentanes. The reaction was also conducted using the linear Polymer 5-5 analogue and the crude oligomeric mixture reported in Section 3.5.4. The results are shown in Table 3.9.

Table 3.9: The chlorination of *o*-cresol using some novel branched polythiaalkanes with comparison to their direct linear analogue.

Catalyst  [Polymer number]		**OC mol%**[b]	**OCOC mol%**[b]	**PCOC Mol%**[b]	***p:o* ratio**	**Mass balance**
A=	**B=**					
pentylene	pentylene	9.2	7.0	81.0	11.6	97.2
pentylene	 [5a]	4.6	8.0	87.7	11.0	100.3
pentylene[c]	 [5b]	7.1	7.7	82.2	10.7	97.0
pentylene	 [6]	4.1	5.9	85.0	14.4	95.0
pentylene	 [7]	8.8	7.2	80.0	11.1	96.0
Oligomer 1		4.0	6.8	86.6	12.7	97.4

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.4.

[b]See Scheme 3.26.

[c]Contains *n*-butyl terminal groups.

From Table 3.9 it is clear that all the polymers tested show a mild enhancement in selectivity relative to the ratio of 6.3 obtained in the baseline result. More notably, there does not appear to be a great disparity observed in the selectivity of the branched polymers, linear polymers and the oligomeric material. However, **Polymer 6** does appear to be the most selective with a ratio of 14.4, but even this is only a mild improvement on the 11.6 observed with the linear reference Polymer 5-5.

The remaining novel linear polythiaalkanes synthesised in this chapter were also tested as catalysts for the chlorination of *o*-cresol and the results are shown in Table 3.10.

Table 3.10: The chlorination of *o*-cresol with sulfuryl chloride in the presence of some novel linear polythiaalkanes.[a]

Catalyst	OC mol%[b]	OCOC mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
5,6	3.5	4.7	86.1	18.3	94.3
5,4	11.1	9.9	72.4	7.3	93.4
5,3	5.5	5.2	84.3	16.2	95.0

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.4.

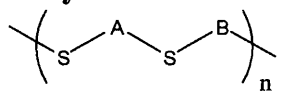
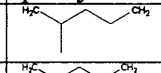
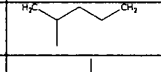
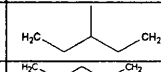
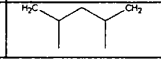
[b]See Scheme 3.26.

Table 3.10 shows that Polymer 5-6 and Polymer 5-3 appear to be relatively good catalysts, and in comparison with the other results displayed here it is difficult to explain this observation. However, the higher selectivities obtained are consistent with other results previously obtained at the Centre for Clean Chemistry.[12] The linear Polymer 5-6 is obviously structurally very similar to the highly selective Polymer 6-6 and therefore would be assumed to react in a similar manner. The linear Polymer 5-3 contains a propylene spacer unit which has been shown to be a very effective entity within the polymer, with numerous polymers containing it having excellent selectivity for the chlorination of *o-cresol* (polymers such as 3-6, 3-9, and 3-12).

3.8.2.2 Chlorination of *o*-cresol using some novel branched polythiaalkanes as catalysts in the absence of a Lewis acid co-catalyst with comparison to their linear analogues.

So far in this thesis, the testing of the sulfide catalysts has only been reported for reactions conducted in the presence of a Lewis acid co-catalyst. However, from a green chemistry and an industrial perspective it is desirable to have a method that excludes the need for the Lewis acids because in general they are regarded as highly corrosive materials which are notorious for damaging industrial process equipment. Therefore, the chlorination of *o*-cresol with these branched polythiaalkanes and their linear analogues was also conducted in the absence of aluminium chloride (Table 3.11 and 3.12).

Table 3.11: Chlorination of *o*-cresol using some novel branched polymers as catalysts in the absence of a Lewis acid with comparison to their direct linear analogue.

Catalyst  [Polymer number]		**OC mol%**[b]	**OCOC mol%**[b]	**PCOC mol%**[b]	***p:o* ratio**	**Mass balance**
A=	**B=**					
pentylene	pentylene	22.1	10.9	62.8	5.8	95.8
pentylene	 [5a]	20.8	14.1	59.0	4.2	93.9
pentylene[c]	 [5b]	1.9	16.9	78.3	4.6	97.1
pentylene	 [6]	1.1	17.7	78.2	4.4	97.0
pentylene	 [7]	5.7	16.5	75.3	4.6	97.5
Oligomer 1		3.0	19.2	71.2	3.7	93.4

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of a polymeric sulfide (0.284 mmol) in the absence of any Lewis acid co-catalyst. For more details see Section 2.15.4.

[b]See Scheme 3.26.

[c]Contains *n*-butyl terminal groups.

Table 3.12: Chlorination *o*-cresol using some novel linear polythiaalkanes in the absence of a Lewis acid.

Catalyst	**OC mol%**[b]	**OCOC mol%**[b]	**PCOC mol%**[b]	***p:o* ratio**	**Mass balance**
5,6	16.7	15.9	66.2	4.2	98.8
5,4	11.4	17.3	63.9	3.7	92.6
5,3	22.6	13.2	57.5	4.4	93.3

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of a polymeric sulfide (0.284 mmol) in the absence of any Lewis acid co-catalyst. For more details see Section 2.15.4.

[b]See Scheme 3.26.

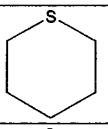
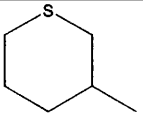
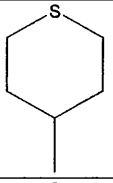
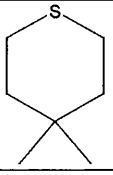
All the results conducted in the absence of the Lewis acid catalyst resulted in values for the selectivity that do not deviate far from the 5.1 observed in the baseline results. This indicates that in the absence of the Lewis acid co-catalyst the sulfide based polymers are completely ineffective as selective catalysts. This can be understood mechanistically, because without the Lewis acid the proposed selective intermediate (chlorosulfonium ion) would not be generated (see Section 1.6). As a result of this investigation it was concluded that the sulfide based polymers synthesised herein require the Lewis acid in order to obtain enhancements in the *para*

selectivity and, therefore, all the remaining chlorination experiments have been conducted in the presence of a Lewis acid.

3.8.2.3 Chlorination of *o*-cresol using tetrahydrothiopyrans as catalysts.

The tetrahydrothiopyrans synthesised in is this chapter were then tested as catalyst for the chlorination of *o*-cresol under the standard conditions. The results are shown in Table 3.13.

Table 3.13 Chlorination of *o*-cresol using tetrahydrothiopyran as catalysts.[a]

Catalyst	OC mol%[b]	OCOC mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
	0.0	2.1	96.4	45.9	98.5
	4.6	2.3	93.6	40.7	100.5
	0.0	2.4	96.6	40.3	99.0
	4.0	2.7	90.0	33.3	96.7

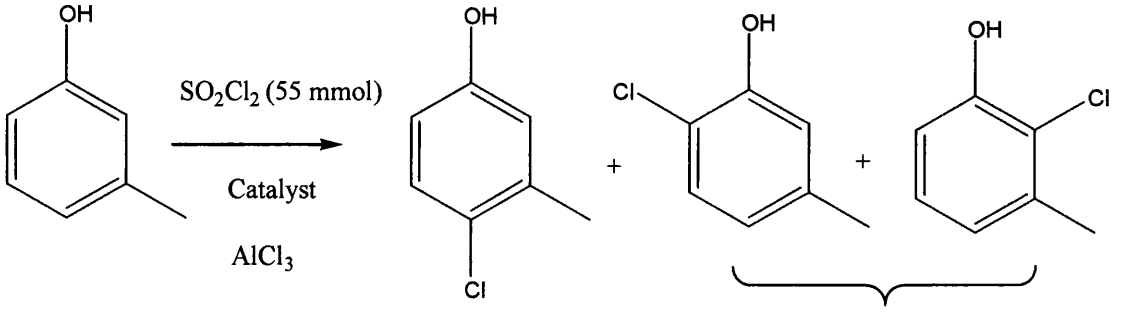
[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a cyclic sulfide (0.284 mmol). For more details see Section 2.15.4.

[b] See Scheme 3.26.

Table 3.13 shows that the tetrahydrothiopyrans that are good catalysts for phenol are excellent catalysts for the chlorination of *o*-cresol. Selectivities in excess of 40 and yields in excess of 95 % for the desired PCOC are obtainable. All of the tetrahydrothiopyrans behave in a similar highly selective manner. This similarity can be understood because the 'top half' of the molecule (the business end), where the functionality lies is the same in each case. Despite the obvious potential these catalysts have for the chlorination of *o*-cresol no further experimentation has been conducted herein due to time constraints.

3.8.3 Chlorination of *m*-cresol.

The polymeric sulfide materials and the cyclic sulfide materials synthesised in this chapter were next tested as potential selective catalysts for the chlorination of *m*-cresol (Scheme 3.37).



MC (50 mmol) **PCMC** **OCMC**

Scheme 3.27: The chlorination of *m*-cresol.

The baseline results for the chlorination of *m*-cresol in the absence of a sulfide catalyst reported in Section 2.15.6 are recorded again in Table 3.14 for ease of reference.

Table 3.14: Baseline results for the chlorination of *m*-cresol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	MC/ mol %[b]	OCMC/ mol %[b,c]	PCMC/ mol %[b]	*p:o* ratio	Mass balance
-	8.7	12.5	78.3	6.3	99.5
$AlCl_3$	14.2	10.0	75.8	7.6	100.0

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (1.875 mmol). For more details see Section 2.15.6.

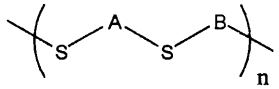
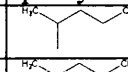
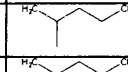
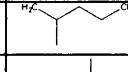
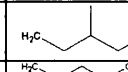
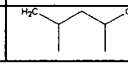
[b] See Scheme 3.27.

[c] Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

3.8.3.1 Chlorination of *m*-cresol using some novel branched polymers as catalysts with comparison to some linear analogues.

Using the standard conditions for *m*-cresol described in Section 2.15.6 the chlorination was conducted in the presence of the branched polymers synthesised from the methyl substituted 1,5-dibromopentanes. The reaction was also conducted using the linear Polymer 5-5 analogue and the crude oligomeric mixture reported in Section 3.5.4. The results are shown in Table 3.15.

Table 3.15: The chlorination of *o*-cresol using some branched polythiaalkanes as catalysts with comparison to their direct linear analogue.[a]

Catalyst  [Polymer number]		**MC/ mol %**[b]	**OCMC/ mol %**[b,c]	**PCMC/ mol %**[b]	***p:o* ratio**	**Mass balance**
A=	**B=**					
pentylene	pentylene	4.7	4.6	89.2	19.4	98.5
pentylene	 [5a]	41.6	4.1	52.7	12.9	98.4
pentylene[d]	 [5a]	6.8	5.3	85.4	16.1	97.5
pentylene [e]	 [5b]	3.9	5.9	89.5	15.2	99.3
pentylene	 [6]	6.7	6.0	78.7	13.1	91.4
pentylene	 [7]	11.7	5.3	80.4	15.2	97.4
Oligomer 1		6.9	7.5	85.3	11.4	99.7

[a]Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the presence of $AlCl_3$ (1.875 mmol) and a polymeric sulfide catalyst (0.403 mmol). For more details see Section 2.15.6.

[b]See Scheme 3.27.

[c]Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

[d]Repeat of the reaction in the above row.

[e]Contains *n*-butyl terminal groups.

Table 3.15 shows that for the chlorination of *m*-cresol it is observed that the linear Polymer 5-5 actually performs more selectively than its branched analogues. A similar observation was apparent in Section 2.15.6 where the branched **Polymers 2** and **4** were shown to be less selective that their linear analogues for the chlorination of *m*-cresol. There appeared to be a problem with the initial reaction in the presence of **Polymer 5a** because 41.6 % of the starting material remained at the end of the

reaction. The reason for such a large amount of starting material to be left unreacted is unknown but when the reaction was repeated only 6.8 % of the starting material remained. It may be that the sulfuryl chloride used in the low yielding experiment had deteriorated.

Despite the fact that under these conditions the branched polymers are less effective as selective catalysts relative to their linear Polymer 5-5 analogue they still show up to a twofold enhancement over the baseline selectivity of 7.6.

The chlorination of *m*-cresol was also carried out in the presence of some novel liner polythiaalkanes and the results are shown in Table 3.16.

Table 3.16 Chlorination of *m*-cresol with some novel linear polymers.[a]

Catalyst	MC/ mol %[b]	OCMC/ mol %[b,c]	PCMC/ mol %[b]	*p:o* ratio	Mass balance
5,6	9.9	4.0	85.1	21.3	99.0
5,4	11.2	6.3	83.1	13.2	100.6
5,3	12.7	5.1	79.2	15.5	97.0

[a]Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the presence of $AlCl_3$ (1.875 mmol) and a polymeric sulfide catalyst (0.403 mmol). For more details see Section 2.15.6.

[b]See Scheme 3.27.

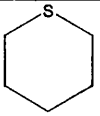
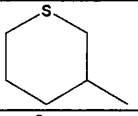
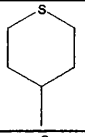
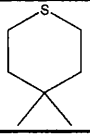
[c]Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

The results in Table 3.16 are similar to the equivalent results for *o*-cresol (see Table 3.10), where Polymers 5,6 and 5,3 are relatively good catalysts (see Section 3.8.2.1).

3.8.3.2 Chlorination of *m*-cresol using tetrahydrothiopyrans as catalysts.

The tetrahydrothiopyrans synthesised as reported in is this chapter were then tested as catalysts for the chlorination of *m*-cresol under the standard conditions. The results are shown in Table 3.17.

Table 3.17 Chlorination of *m*-cresol using tetrahydrothiopyran as catalysts.[a]

Catalyst	MC/ mol %[b]	OCMC/ mol %[b,c]	PCMC/ mol %[b]	*p:o* ratio	Mass balance
	4.3	5.7	89.6	15.7	99.6
	7.9	5.2	82.9	15.9	96.0
	15.4	4.5	78.4	17.4	98.3
	4.7	4.7	90.4	19.2	99.8

[a]Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the presence of $AlCl_3$ (1.875 mmol) and a cyclic sulfide catalyst (0.403 mmol). For more details see Section 2.15.6.

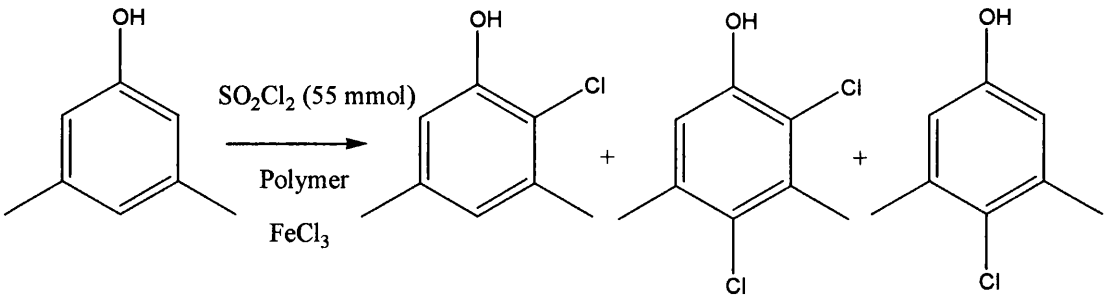
[b]See Scheme 3.27.

[c]Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

From Table 3.17 it can be seen that the tetrahydrothiopyrans appear to be moderately good catalysts for *m*-cresol. However, unlike the results obtained for phenol and *o*-cresol, these cyclic catalysts are not considerably more selective than the tested polymeric materials. In fact, the chlorination of *m*-cresol in the presence of Polymer 5-5 and 5-6 gives rise to marginally higher selectivity values than these presented here, with values of 19.4 and 21.3 respectively (see Tables 3.15 and 3.16).

3.8.4 Chlorination of *m*-xylenol.

The polymeric sulfide materials and the cyclic sulfide materials synthesised in this chapter were next tested as potential selective catalysts for the chlorination of *m*-xylenol (Scheme 3.28).



MX (50 mmol) **OCMX** **DCMX** **PCMX**

Scheme 3.28: The chlorination of *m*-xylenol.

The baseline results for the chlorination of *m*-xylenol in the absence of a sulfide catalyst reported in Section 2.15.8 are recorded again in Table 3.17 for ease of reference.

Table 3.17: Baseline results for the reaction of *m*-xylenol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	MX/ mol %	OCMX/ mol %	PCMX/ mol %	DCMX/ mol %	*p:o* ratio	Mass balance
-	13.4	9.8	68.6	0.0	7.0	91.8
$FeCl_3$	15.4	10.3	71.1	0.0	6.9	96.8

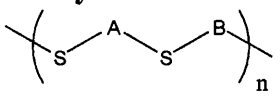
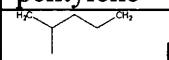
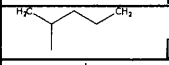
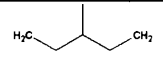
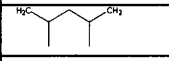
[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $FeCl_3$ (0.154 mmol). For more details see Section 2.15.8.

[b] See Scheme 3.17.

3.8.4.1 Chlorination of *m*-xylenol using some novel branched polymers as catalysts with comparison to their linear analogues.

Using the standard conditions for *m*-xylenol described in Section 2.15.8 the chlorination was conducted in the presence of the branched polymers synthesised from the methyl substituted 1,5-dibromopentanes. The reaction was also conducted using the linear Polymer 5-5 analogue and the crude oligomeric mixture reported in Section 3.5.4. The results are shown in Table 3.18.

Table 3.18: Chlorination of *m*-xylenol using some novel branched polymers with comparison to their direct linear analogue.[a]

Catalyst  [Polymer number]		**MX/ mol %** [b]	**OCMX/ mol %** [b]	**PCMX/ mol %** [b]	**DCMX/ mol %** [b]	***p:o* ratio**	**Mass balance**
A=	**B=**						
pentylene	pentylene	19.7	8.0	67.0	0.8	8.4	95.5
pentylene	 [5a]	6.2	12.8	77.9	1.7	6.1	98.6
pentylene[c]	 [5b]	4.3	12.2	80.8	1.5	6.6	98.8
pentylene	 [6]	16.7	10.3	71.0	0.6	6.9	98.6
pentylene	 [7]	10.3	12.1	68.5	4.0	5.7	94.9
Oligomer 1		15.2	15.2	62.7	0.0	4.1	93.1

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) and a polymeric sulfide catalyst (0.052 mmol). For more details see Section 2.15.8

[b] See Scheme 3.17.

[c] Contains *n*-butyl terminal groups.

Table 3.18 strongly suggests that the branched polymers synthesised in this chapter are very poor catalysts for the chlorination of *m*-xylenol. These results are in sharp contrast to the highly selective branched catalyst (**Polymer 2**) reported in chapter 2. The reason for this may be that the active sulfur atoms in **Polymer 2** were considerably more hindered for two reasons - firstly there is a branched spacing group on both sides of the sulfur and secondly the branching is on the alpha carbon atoms. In **Polymers 5** to **7** each sulfur is connected to one branched spacing group and one linear spacing group, and the actual branching is located further away from the sulfur atom, at the beta or gamma carbons. Therefore, it is conceivable that the lower degree of steric hindrance observed in **Polymers 5** to **7** do not allow them to proceed by the selective mechanism proposed for **Polymer 2** (see Section 2.15.12).

Table 3.18 also shows that all the branched compounds are in fact marginally less selective that the linear Polymer 5-5 reference catalyst.

The chlorination of *m*-xylenol was also conducted in the presence of some other novel linear polythiaalkanes and the results are shown in Table 3.19.

Table 3.19: Chlorination of *m*-xylenol with some novel linear polymers.[a]

Catalyst	MX/ mol %	OCMX/ mol %	PCMX/ mol %	DCMX/ mol %	*p:o* ratio	Mass balance
5,6	5.8	6.8	82.1	1.9	12.1	96.6
5,4	14.4	9.1	65.2	6.1	7.2	94.8
5,3	10.1	6.0	82.4	0.9	13.7	99.4

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) and a polymeric sulfide catalyst (0.052 mmol). For more details see Section 2.15.8

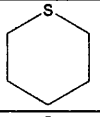
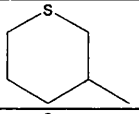
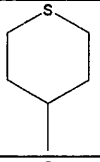
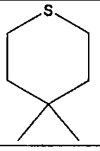
[b] See Scheme 3.17.

These novel linear polymers are also shown to be more selective than the branched **Polymers 5** to **7**, and once again the linear Polymers 5-6 and 5-3 obey the trend and prove to be more selective than the Polymer 5-4 (see Section 3.8.2.1)

3.8.4.2 Chlorination of *m*-xylenol using tetrahydrothiopyrans as catalysts.

The tetrahydrothiopyrans synthesised in is this chapter were then tested as catalysts for the chlorination of *m*-xylenol under the standard conditions. The results are shown in Table 3.20.

Table 3.20: Chlorination of *m*-xylenol using various tetrahydrothiopyrans.

Catalyst	MX/ mol %	OCMX/ mol %	PCMX/ mol %	DCMX/ mol %	*p:o* ratio	Mass balance
	2.8	6.6	89.1	0.7	13.5	99.2
	7.1	8.7	78.1	2.9	9.0	96.8
	15.4	27.7	53.8	0.0	1.9	96.9
	5.8	19.7	73.6	0.0	3.7	99.1

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) and a cyclic sulfide catalyst (0.052 mmol). For more details see Section 2.15.8

[b] See Scheme 3.17

Table 3.20 shows that the tetrahydrothiopyrans that have been shown to be good catalysts for phenol and *m*-cresol and excellent catalyst for *o*-cresol are surprisingly poor catalysts for *m*-xylenol. Also, unlike the results with phenol, *o*-cresol and *m*-cresol in this table there appears to be a large disparity in the reactivity of the tetrahydrothiopyrans, with the non substituted ring giving by far the highest *p:o* ratio and rings with the substitution at the 4 position giving very low *p:o* ratios, which are even low relative to the baseline results.

These findings are very interesting and are at the moment very difficult to explain. No further investigations have been conducted here due to time constraints.

3.9 Conclusion for chapter 3

Several semi branched polymers containing pentylene spacing units have been synthesised from various 1,5-dibromopentanes and have been shown to be relatively poor catalysts for the selective chlorination of phenols.

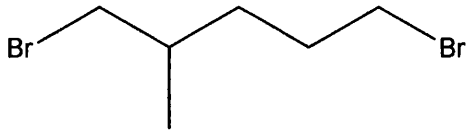
Several methyl-substituted tetrahydrothiopyrans have also been synthesised and have all shown to be good selective catalysts for phenol and *m*-cresol and highly selective catalysts for *o*-cresol.

3.10 Experimental

3.10.1 Synthesis of 1,5-dibromo-2-methylpentane

In a 100 mL round bottomed flask was placed 3-methyltetrahydropyran (5.00 g, 49.9 mmol) and HBr (15.0 g, 59.7 mmol, 48 %). H_2SO_4 (4.90 g, 49.9 mmol) was added slowly over 15 minutes. The reaction was heated to 130°C and allowed to stir for 2 h. The reaction was cooled. Dichloromethane (50 mL) was added. Extraction was undertaken followed by separation. The extraction process was repeated twice more. The organic phase was dried over $MgSO_4$. The drying agent was then filtered off. The solvent was removed by rotary evaporation to give a thick black oil (9.71 g). The oil was subjected to kugelrohr distillation (2mmHg). One fraction (35°C, 0.65 g) was obtained and was a clear liquid, which was probably the 3-methyltetrahydropyran starting material. A second fraction (95°C, 5.20 g) was obtained and was a dark

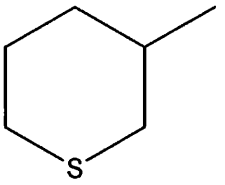
brown coloured oil. This oil was kugelrohr distilled twice more to give a slightly yellow coloured oil (4.21 g, 35 % yield). Lit.[13] 117°C at 12 mmHg.



^{1}H-NMR ($CDCl_3$) δ 1.00 (3H, d, J = 6.5 Hz, CH_3), 1.30-2.30 (5H, m ,$CH(CH_3)CH_2CH_2$), 3.3-3.6 (4H, m, 2 x $BrCH_2$).^{13}C-NMR ($CDCl_3$) δ 19.1 (CH_3), 30.8 (CH_2), 33.8 (CH_2), 33.8 (CH_2), 33.9 (CH), 41.3 ($BrCH_2$). FTIR (neat) *v* 649 (C-Br str). MS EI$^+$ m/z 165 ([(M 2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{79}Br,^{81}Br)-^{79}Br]$^+$ 30 %), 163 ([M(2 x ^{79}Br)- Br^{79}]$^+$/ [M (^{79}Br, ^{81}Br)- ^{81}Br]$^+$ 30 %), 83 ([M-HBr-Br]$^+$ 100 %), 69 ($C_5H_9^+$, 65 %).

3.10.2 Attempted polymer formation from 1,5-dibromo-2-methylpentane and sodium sulfide by Method B. Synthesis of 3-methyltetrahydrothiopyran.

1,5-Dibromo-2-methylpentane (4.01 g, 16.4 mmol) and $Na_2S.9H_2O$ (7.88 g, 32.78 mmol) were placed in a 20 mL round bottomed flask fitted with a reflux condenser. The reaction was heated to 170 °C for 7 h. The reaction was allowed to cool. Water (20 mL) and dichloromethane (20 mL) were then added to the residue and extraction was then undertaken. The aqueous phase was re-extracted with dichloromethane (3 x 20 mL). The combined organic phases were dried over $MgSO_4$. The drying agent was then filtered off. The solvents were removed by rotary evaporation to give an oily crude product (2.00 g). The crude product was subjected to kugelrohr distillation. One fraction which distilled at 70 °C and 20mmHg (1.44 g, 75 %) was obtained as a clear, colourless, odorous oil and confirmed as the title compound. Lit.[13] 158°C at ambient pressure.



^{1}H-NMR ($CDCl_3$) δ 0.89 (3H, d, J = 6.5 Hz, CH_3), 1.6-2.0 (5H, m, $CH(CH_3)CH_2CH_2$), 2.2-2.5 (4H, m, SCH_2).^{13}C-NMR ($CDCl_3$) δ 23.1 (CH_3), 28.1 ($CH_2CH(CH_3)$), 28.8 ($CH_2CH_2CH_2$), 33.5 (CH), 36.1, 35.2, (SCH_2). FTIR (neat) *v* 669 (possibly C-S str). MS EI$^+$ m/z 116 ($[M]^+$ 90), 101 ($[M-CH_3]^+$, 100 %). HRMS EI$^+$ m/z calcd for $[M]^+$ 116.0654, found. 116.0654.

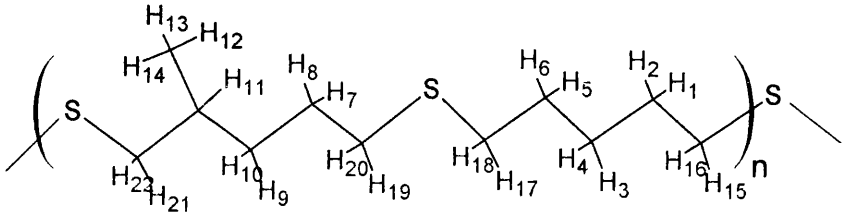
3.10.3 Synthesis of Polymers 5a and 5b from 1,5-dibromo-2-methylpentane and 1,5-pentanedithiol by Method A.

1,5-Pentanedithiol (2.00 ml, 15 mmol) and dry THF (20 mL) were added to a dry 100 mL round bottomed flask *via* a dry syringe. The flask was flushed with N_2 and the atmosphere was maintained during the course of the reaction. The flask was cooled to -78°C using a dry ice and acetone bath. Butyllithium (2.5 M, 12 mL, 30 mmol) was added slowly over 20 minutes. The reaction was allowed to proceed for 30 minutes, and was then allowed to warm to room temperature. 1,5-Dibromo-2-methylpentane (3.66 g, 15 mmol) was added *via* a dry syringe and the reaction was left to proceed for 20 h. The reaction was quenched with water (20 mL). No insoluble precipitate was present. Dichloromethane (40 mL) was added and extraction was undertaken. The aqueous phase was re-extracted 5 times with dichloromethane (5 x 30 mL). The organic phases where combined and dried over $MgSO_4$. The drying agent was then filtered off. The solvent was removed by rotary evaporation and then the crude oil was dried in a vacuum oven (40°C, 1 mmHg) for 24 h to give a thick yellow oil (2.23 g, 68 %).

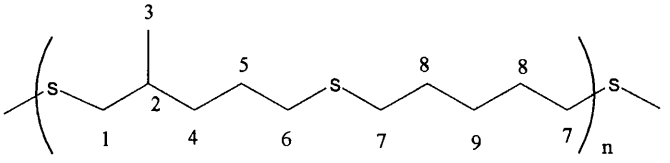
Polymer formation using n-bromobutane as a terminating group.

1,5-Pentanedithiol (2.00 ml, 15 mmol) and dry THF (20 mL) were injected into a dry 100 mL round bottomed flask, which was flushed with N_2. The flask was cooled to -78°C using dry ice and acetone. Butyllithium (2.5M, 12 mL, 30 mmol) was added slowly over 20 minutes. The reaction was allowed to proceed for 30 minutes; then allowed to warm to room temperature.

1,5-Dibromo-2-methylpentane (3.30 g, 13.5 mmol) was added *via* a dry syringe and the reaction was left to proceed for 1 h. 1-Bromobutane (0.42 g, 3 mmol) was then added and the reaction was left to proceed for 20 h. The reaction was quenched with water (20 mL). No insoluble precipitate was present. Dichloromethane (40 mL) was added and extraction was undertaken. The aqueous phase was re-extracted 5 times with dichloromethane (5 x 30 mL). The organic phases were combined and dried over $MgSO_4$. The drying agent was then filtered off. The solvent was removed by rotary evaporation to give a crude oil. Any remaining volatile material was removed by reduced pressure distillation (100 °C, 2mmHg) to give a slightly yellow oil (2.81 g, 86 %).



^{1}H-NMR ($CDCl_3$) δ 1.00 (3H, d, J = 6.5 Hz, H12-H14), 1.30-2.30 (11H, m, H1-H11), 2.40-3.40 (8H, m, H15-H22).



As previously mentioned the unsymmetrical 1,5-dibromo-2-methylpentane can react to form a spacer group with two different orientations. Using the figure shown above the methyl group could be on C2 (as shown) or on C5 position. This observation informs us that the linear pentylene spacing group (C7-C9) is actually not made up of 3 distinct carbon environments and that the 2 C7s and 2 C8s are technically different as they are potentially connected to two differently oriented groups. However the ^{13}CNMR spectrum gave rise to only 9 signals, and therefore it can be assumed that both orientations actually result in no significant difference on the magnetic environment of the corresponding C7 and C8 carbons.

^{13}C-NMR ($CDCl_3$) δ 19.8 (C3), 27.4, 28.0, 29.8, 32.5, 33.2, 33.6, 35.9, 40.3 (C1, C2, C4-C9). FTIR (neat) *v* 734 (possibly C-S). No C-Br str a. GPC M_n 2440 (without terminating group), 705 (with terminating group).

3.10.4 Synthesis of 3-methyl-1,5-pentanediol

Lithium aluminium hydride reduction

In a 50 mL oven dried round bottomed flask was placed $LiAlH_4$ (0.95 g, 25.0 mmol) and dry THF (37.5 mL). The flask was flushed with N_2. A solution of 3-methylglutaric acid (1.5 g, 10.3 mmol) in dry THF (12.5 mL) was added in a drop-wise manner to the lithium aluminium hydride solution over a period of 30 minutes. The mixture was allowed to stir for 4 h and it was observed that after 1 h there was a significant amount of a white precipitate formed. Water was added in a drop-wise manner until no further effervescence occurred. The inorganic precipitate formed was filtered off by suction filtration, and was then washed through with ether (50 mL) and water (50 mL). The phases were then separated and the organic phase was dried over $MgSO_4$. The drying agent was filtered off and the solvents were removed by rotary evaporation to give an oily residue (40 mg). The oil was distilled by kugelrohr distillation (100-140°C, 2mmHg) to give a clear oil (32 mg). The oil was analysed by GC and NMR to show a mixture of 2 compounds, one of which was later confirmed to be the desired diol and the other component was likely to be 3-methylpent-4-en-1-ol. The unsaturated alcohol was assumed to be the second component due to the presence of protons in the alkene region in the NMR and the shorter retention time in the GC. The water was removed from the aqueous phase by rotary evaporation and the resulting residue (0.56 g) was subjected to kugelrohr distillation. One component (130-140°C, 2mmHg) was obtained (0.46 g, 38 %). Lit.[14] 111-113°C at 1mmHg.

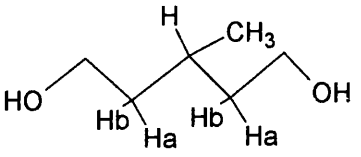
The above procedure was repeated but the scale was doubled.

The desired diol (0.98 g, 41 %) was isolated in the same manner.

Diborane reduction method

Boron trifluoride diethyl etherate (1.6 mL, 10.0 mmol) in dry THF (50 mL) was added slowly to an oven dried 100 mL round bottomed flask containing 3-methylglutaric acid (1.0 g, 6.84 mmol), $NaBH_4$ (0.90g, 23.9 mmol) and dry THF (50 mL). The mixture was then refluxed and followed by thin layer chromatography

until all the starting material was consumed. This took approximately 6 h. The vessel was allowed to cool and was then quenched with water (25 mL). The solvents were removed by rotary evaporation. Diethyl ether (50 mL) was then added and the mixture was stirred vigorously for 2 h. The ether was decanted. More ether (25 mL) was added to the vessel and the reaction was allowed to stir vigorously for another hour to dissolve any diol product. The ether was then decanted and combined with the previously decanted ether and was then dried other $MgSO_4$. The drying agent was filtered off and the solvent was removed by rotary evaporation. The crude product (1.13 g) was subjected to reduced pressure distillation and a clear colourless thick oil (0.75 g, 93 %) was isolated (130-140°C, 2mmHg). Lit.[14] 111-113°C at 1mmHg.



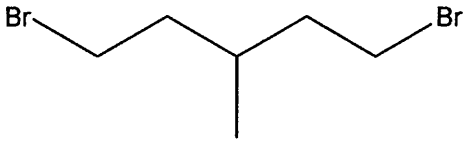
^{1}H-NMR ($CDCl_3$) δ 0.72 (3H, d, J = 6.5 Hz, CH_3), 1.20 (2H, m, $CH_a(H_b)CH(CH_3)CH_a(H_b)$), 1.38 (2H, m, $CH_a(H_b)CH(CH_3)CH_a(H_b)$), 1.60 (1H, m, $CHCH_3$), 2.40 (2H, s, OH, D_2O exchangeable), 3.50 (4H, m, 2 x $HOCH_2$). ^{13}C-NMR($CDCl_3$) δ 20.3 (CH_3), 26.3 (CH), 39.8 (CH_2), 60.9 ($HOCH_2$). FTIR (neat) *v* 3295 (OH *str*), 1050, 1010 (C-O *str* and O-H *def*). MS $CI^+(NH_3)$ m/z 136 ($[M+NH_4]^+$ 100 %), 132 (70 %).

3.10.5 Synthesis of 1,5-dibromo-3-methylpentane.

In a 10 mL round bottomed flask fitted with a reflux condenser was placed HBr (2.86 mL, 16.9 mmol, 48 %). The flask was cooled externally by an ice bath. Concentrated sulfuric acid (1.81 mL, 34 mmol) was then added cautiously in a drop-wise manner. 3-Methyl-1,5-pentanediol (1.00 g, 8.5 mmol) was added slowly. The reaction was left to stir overnight. The reaction was heated on a water bath for 3 h before being left to cool. The organic components were extracted with dichloromethane (15 mL x 2). The organic phases were combined and washed with water (30 mL), 10 % Na_2CO_3 (30 mL), and then dried over $MgSO_4$. The drying agent

was filtered off and the solvents were removed by rotary evaporation, to give a brown coloured crude oil (1.81 g).

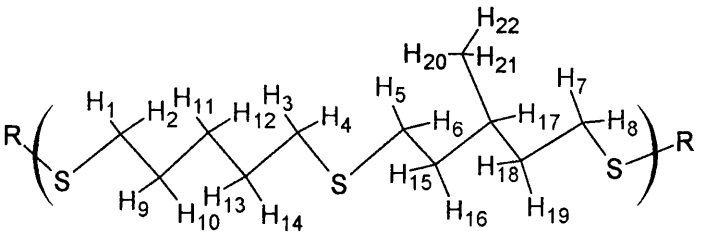
TLC analysis of the oil indicated 3 components; 1 corresponded to the starting material; another had an Rf similar to 1,5-dibromo-2-methylpentane and was likely to be the desired product. The third spot had an Rf in between the other spots and may correlate to 5-bromo-3-methylpentan-1-ol. Column chromatography was undertaken. One fraction (1.72 g, 83 %) was isolated as a clear clourless oil.



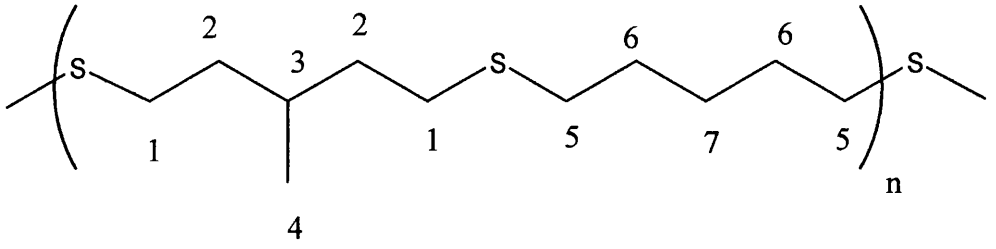
^{1}H-NMR ($CDCl_3$) δ 0.75 (3H, d, J = 6.5 Hz, CH_3), 1.45-1.85 (5H, 2m, $CH_2CH(CH_3)CH_2$), 3.25 (4H, m, 2 CH_2Br).^{13}C-NMR ($CDCl_3$) δ 18.6 (CH_3), 31.0 (CH), 31.7 (CH_2), 39.8 ($BrCH_2$). FTIR (neat) *v* 662, 641 (C-Br str). MS EI$^+$ m/z 165 ([(M 2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{79}Br,^{81}Br)-^{79}Br]$^+$,10 %), 163 ([M(2 x ^{79}Br)- Br^{79}]$^+$/ [M(^{79}Br, ^{81}Br)-^{81}Br]$^+$,8 %), 95 ([$CH_2{}^{81}$Br]$^+$, 90 %), 93.0 ([$CH_2{}^{79}$Br]$^+$,100 %), 81 ([^{81}Br]$^+$, 65 %), 79 ([^{79}Br]$^+$, 55 %), 55 (C_4H_7, 90 %). HRMS EI$^+$ m/z calcd for [M(2x^{79}Br)]$^+$ 241.9300, found 241.9299.

3.10.6 Synthesis of poly(sulfanediyl-3-methylpentane-1,5-diylsulfanediylpentane-1,5-diyl) (Polymer 6) from 1,5-dibromo-3-methylpentane by Method A.

The standard Method A polymer forming step utilising *n*-bromobutane as a terminating group was undertaken. The procedure is described in Section 3.10.3. The amounts of reagents used were as follows: 1,5-pentanedithiol (1.00 ml, 7.5 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), 1,5-dibromo-3-methylpentane (1.65 g, 6.75 mmol) and 1-bromobutane (0.41 g, 3 mmol). The crude product was removed from any volatile components by heating to 100°C at 2mmHg pressure to give the final clear colourless oil product (1.06 g, 65 %).



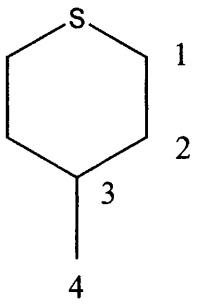
^{1}H-NMR ($CDCl_3$)δ 0.65-0.9 (3H, H20-H22), 1.00-1.50 (11H, H9-H19), 2.2-3.5 (8H, H1-H8).



^{13}C-NMR ($CDCl_3$) δ 19.5 (C4), 30.0 (C3), 28.6, 29.7, 32.6 (C2, C6, C7) 37.0, 37.3 (C5, C1) FTIR (neat) *v* 738 (possibly C-S). No C-Br str. GPC M_n 2090.

3.10.7 Synthesis of 4-methyltetrahydrothiopyran.

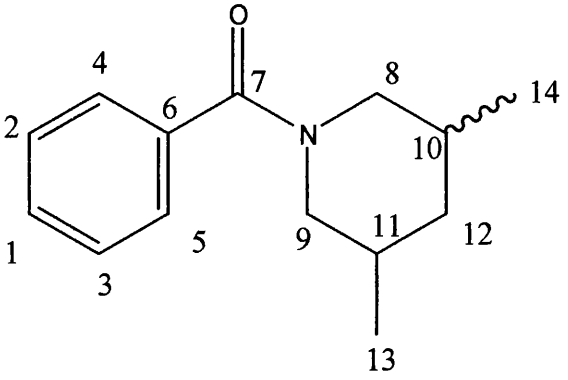
1,5-Dibromo-3-methylpentane (1.00 g, 4.1 mmol) and $Na_2S.9H_2O$ (1.48 g, 6.1 mmol) were placed in a 20 mL round bottomed flask fitted with a reflux condenser. The mixture was heated to 170°C for 5 h. The reaction was allowed to cool, water (20 mL) and dichloromethane (20 mL) were then added to the residue and extraction was undertaken. The aqueous phase was re-extracted with dichloromethane (3 x 20 mL). The combined organic phases were dried over $MgSO_4$. The drying agent was then filtered off. The solvents were removed by rotary evaporation to give an oily crude product (0.40 g). The crude product was subjected to kugelrohr distillation. One fraction (0.377 g, 79 %) was obtained as a clear oil at 50-55°C at 20mmHg. Lit.[13] 54°C at 22 mmHg.



^{1}H-NMR ($CDCl_3$) δ 0.85 (3H, d, J = 6 Hz, CH_3), 1.10-1.40 (4H, m, $C2H_2$), 1.90 (1H, m, CH), 2.45-2.55 (4H, m, 2 x CH_2S). ^{13}C-NMR ($CDCl_3$) δ 23.4 (C4), 29.2 (C2), 32.6 (C3), 36.3 (C1). FTIR (neat) *v* 662 (possibly C-S str). MS EI$^+$ m/z 116 ($[M]^+$, 100 %), 101 ($[M-CH_3]^+$, 95 %), 67 ($[C_5H_7]^+$, 90%), 41 ($[C_3H_5]^+$, 85 %). HRMS EI$^+$ m/z calcd for $[M]^+$ 116.0654, found.116.0653.

3.10.8 Synthesis of Von Braun amide.

NaOH (2.625 g, 65 mmol) dissolved in water (20 mL) was placed in a 100 mL round bottomed flask. 3,5-Dimethylpiperidine (5.66 g, 50 mmol) was added to the basic solution. Benzoyl chloride (5.78 g, 50 mmol) was added slowly over 2 h *via* a dropping funnel. A yellow precipitate formed. The aqueous phase was extracted with toluene (50 mL x 2). The toluene extract was dried over $MgSO_4$. The toluene was removed by rotary evaporation to give a crude white/yellow solid. The solid was dissolved in methanol, and re-precipitated by the addition of water. The resulting white solid (12.15 g) was collected by suction filtration. IR analysis of the solid showed the expected bands, but also a band at 3200-3400 indicating residual piperidine. TLC analysis confirmed this. The remaining piperidine starting material was distilled from the solid by heating the solid to 80 °C at 19 mmHg of pressure. The resulting solid was re-crystallised from hot ethanol to give white crystals (10.11 g, 93 %). The reaction was repeated twice and in these reactions any remaining piperidine starting material was removed by washing with HCl (1M) instead of by distillation. Yields of 94 % and 95 % were obtained.



Mix of *cis* and *trans* isomers;
Isomer 1a and 1b.

There were 2 isomers present due to the mixture of *cis*- and *trans*-dimethylpiperidine starting material. GC showed that there was one major isomer (**Isomer 1a**) and one minor isomer (**Isomer 1b**). The ratio of 1a:1b was ≈ 5.

Isomer 1a

^{13}C-NMR ($CDCl_3$) δ 19.3 ,19.5 (C13, C14), 31.5, 32.6 (C10, C11), 42.9 (C12), 49.5, 55.2 (C8, C9) 127.2, 127.3 (C5, C4), 128.8, 128.8 (C3, C2) 129.8 (C1), 137.1 (C6), 170.4 (C7).

Isomer 1b

^{13}C-NMR ($CDCl_3$) δ 18.2, 18.8 (C13, C14), 26.9, 28.3 (C10, C11), 39.8 (C12), 49.2, 54.3 (C8, C9), 127.2, 127.3 (C5, C4), 128.8, 128.8 (C3, C2), 129.8 (C1), 137.0 (C6), 171.4 (C7).

Due to the existence of these two isomers and the diastereotopic nature of protons adjacent to the asymmetric centres within these 2 isomers the proton NMR appears as a complicated mixture of many different signals and therefore provides limited information for the assignment of structure. No coupling constant values were obtainable and therefore the two isomers have not been assigned as *cis*- or *trans*-.
FTIR (neat) *v* 1617 (C=O str). MS EI$^+$ m/z 217 ([M]$^+$, 15 %), 216 ([M-H]$^+$, 40 %), 202 ([M-CH_3]$^+$, 15 %), 105 ([C_6H_5C=O]$^+$, 100 %), 77 ([C_6H_5]$^+$, 90 %). HRMS EI$^+$ m/z calcd for [M+H]$^+$, 218.1539, found 218.1541.

3.10.9 Synthesis of 1,5-dibromo-2,4-dimethylpentane.Von Braun degradation.

A mixture of *cis*- and *trans*-*N*-benzoyl-3,5-dimethylpiperidine (8.02 g, 36.8 mmol) was dissolved in dichloromethane (24 mL) and placed in a three necked round bottomed flask equipped with an addition funnel, thermometer, magnetic stirrer and a nitrogen inlet system. Phosphorus tribromide (3.50 mL , 36.8 mmol) was added from the addition funnel slowly over 2 h, ensuring the temperature remained below 25°C. Liquid bromine (5.88 g, 36.8 mmol) was then added slowly from a new addition funnel over 4 h, once again ensuring the exothermic reaction did not allow the temperature to exceed 25°C. The addition funnel was removed and the reaction was heated to 90°C for 2 h in order to remove any remaining bromine. The mixture was allowed to cool and was left overnight. The resulting thick red oil was distilled at 130-150°C at 4mmHg pressure. The distillate was assumed to contain oxyphosphorus tribromide, benzonitrile and the dibromopentane. The distillate was poured carefully onto ice (30 g) and left to stir for 2 h in order to decompose the oxyphosphorus tribromide. The resulting aqueous material was extracted with hexane (30 mL x 2). The hexane layers were removed and were washed with concentrated sulfuric acid (2 mL x 5) in order to convert the benzonitrile to benzoic acid. The hexane layer was then washed with a saturated Na_2CO_3 solution (30 mL x 2) and then washed with water (30 mL). The hexane layer was removed and dried over $MgSO_4$. The drying agent was removed by filtration and the solvent was removed by rotary evaporation to give a crude brown oil (0.87 g). The oil was subjected to kugelrohr distillation at 4 mmHg. One fraction (0.78 g, 8 %) was obtained at 110-135 °C as a colourless oil. Lit.[15] 72-73 °C at 2 mmHg.

Alternative procedure[9]

N-Benzoyl-3,5-dimethylpiperidine (8.00 g, 36.8 mmol) was placed in a three necked round bottomed flask equipped with an addition funnel, thermometer, magnetic stirrer and a nitrogen inlet system. Phosphorus tribromide (3.50 mL, 36.8 mmol) was added from the addition funnel slowly over 45 minutes, ensuring that the temperature remained below 25°C. Liquid bromine (5.88 g, 36.8 mmol) was added from a new addition funnel slowly over 2 h, once again ensuring the exothermic reaction did not allow the temperature to exceed 25°C. The addition funnel was removed and the mixture was heated to 90°C for 2 h in order to remove any remaining bromine. The reaction was allowed to cool. The thick red oil was

distilled at 130-150°C at 4mmHg. The resulting distillate was assumed to contain oxyphosphorous tribromide, benzonitrile and the dibromopentane. The distillate was poured carefully onto ice (30 g) and left to stir for 2 h in order to decompose the oxyphosphorous tribromide. Hydrobromic acid (30 mL) was added to the aqueous mixture and the resulting mixture was then refluxed for 4 h. The organic components were extracted with dichloromethane (2 x 50 mL). The dichloromethane layer was then washed with saturated Na_2CO_3 solution (50 mL x 3) and water (50 mL). The organic phase was removed and dried over $MgSO_4$. The solvents were removed by rotary evaporation to give a crude brown oil (1.93 g). The oil was subjected to kugelrohr distillation at 4mmHg. One fraction (1.72 g, 18.5 %) was obtained at 115-140 °C. Lit.[15] 72-73 °C at 2 mmHg.

Due to the use of a mixture of *cis*- and *trans*-3,5-dimethylpiperidine in the first synthetic step the dibromo compound was also a mixture of geometric isomers. The dibromide existed as two different compounds. The first was a meso compound, with both methyl branches on the same side of the molecule. This compound has a mirror plane of symmetry (σ). The second compound has the methyl groups on opposite sides of the molecule. However, these two methyl groups as well as the surrounding groups are equivalents due to C_2 symmetry that exists in the molecule. These observations are illustrated in Figure 3.7.

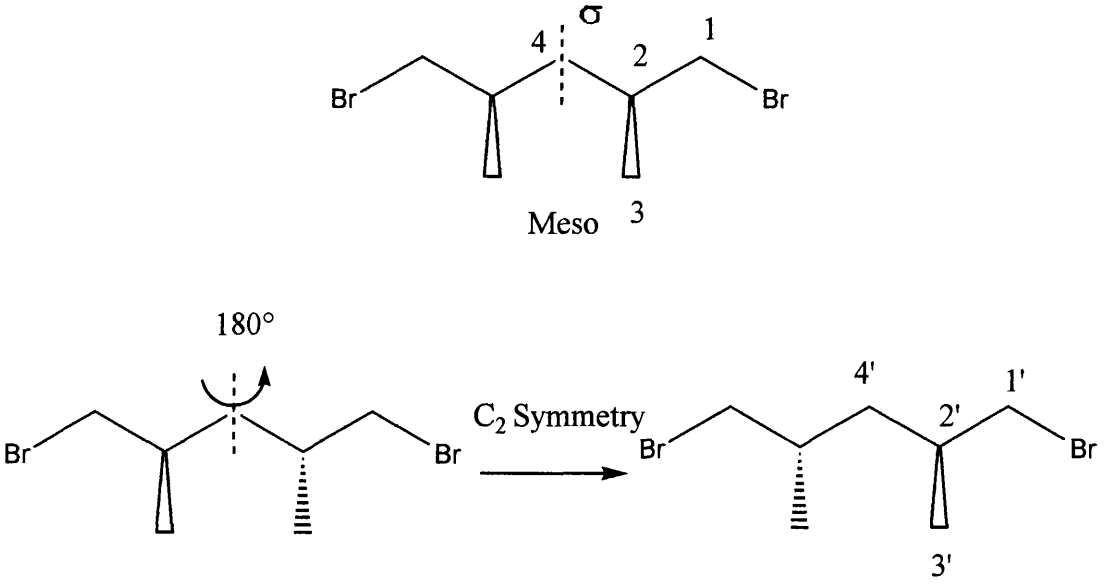
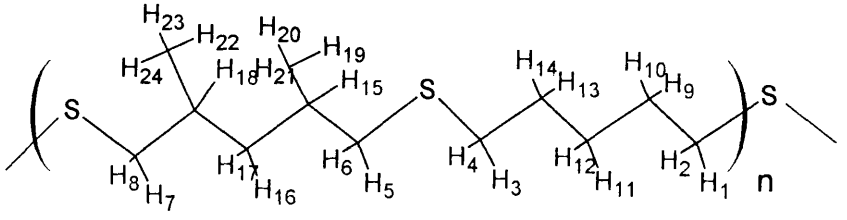


Figure 3.7: Mixture of geometric isomers of 1,5-dibromo-2,4-dimethylpentane. The carbons have been numbered to distinguish between magnetically different carbons.

^{1}H-NMR ($CDCl_3$)δ 1.00-1.15 (6H, 2 x d, J = 6.5, and 6.5 Hz, 2 x CH_3), 1.90-2.10 (2H, m, CH), 1.30-1.60 (2H, m, $C4H_2$), 3.40-3.60 (4H, m, CH_2Br).^{13}C-NMR ($CDCl_3$) δ 18.6, 18.9 (C3 and C3'), 33.2, 32.7 (C2, C2'), 40.7, 40.5 (C4, C4'), 41.9, 41.5 (C1, C1'). FTIR (neat) *v* 641, 661 (C-Br str).

3.10.10 Synthesis of poly(sulfanediyl-2,4-dimethylpentane-1,5-diylsulfanediylpentane-1,5-diyl) (Polymer 7)

The standard Method B polymer forming step utilising *n*-bromobutane as a terminating group was undertaken. The procedure is described in Section 3.10.3. The amounts of reagents used were as follows: 1,5-pentanedithiol (1.00 ml, 7.5 mmol), dry THF (20 mL), butyllithium (2.5M, 6 mL, 15 mmol), 1,5-dibromo-2,4-dimethylpentane (1.75 g, 6.75 mmol) and 1-bromobutane (0.21 g, 1.5 mmol). The crude product was dried under reduced pressure (2mmHg, 60°C) overnight to yield a thick clear colourless oil (0.98 g, 56 %).



^{1}H-NMR ($CDCl_3$) δ 0.80-1.20 (6H, m, H19-H24), 1.20-1.85 (10H, m, H9-H18), 2.10-3.60 (8H, m, H1-H8). FTIR (neat) *v* 747 (possibly C-S). No C-Br str. GPC M_n 1230.

3.10.11 Synthesis of 3,3-dimethylpentanediol

Lithium aluminium hydride reduction of 3,3-dimethylglutaric acid.

The reaction procedure described in Section 3.10.4 was followed. The crude product was then subjected to reduced pressure distillation at 2 mmHg. One fraction (0.68 g, 51 %) was isolated at 130-160°C as a thick clear colourless oil.

Adapted lithium aluminium hydride procedure.

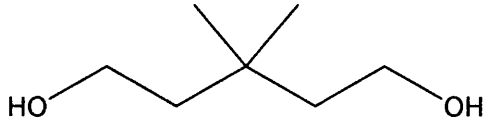
In a 200 mL 3 necked oven dried round bottomed flask equipped with a magnetic stirrer a pressure equalising dropping funnel and a nitrogen inlet system was

placed $LiAlH_4$ (1.90 g, 50.0 mmol) and dry THF (100 mL). The mixture was then refluxed. A solution of 3,3-dimethylglutaric acid (3.22 g, 20 mmol) in dry THF (25 mL) was added in a drop-wise manner *via* the addition funnel over a period of 1 h. The reaction was allowed to reflux for 12 h. After 2 h a white precipitate formed. NaOH (1M) was added in a drop-wise manner until no further effervescence occurred ($\approx$ 25 mL). The reaction was allowed to stir for 2 h. A white granular precipitate formed. The inorganic components were filtered off. The solvents (THF and some excess water) were removed by rotary evaporation. The crude product was dissolved in ether and was then dried over $MgSO_4$. The drying agent was filtered off and the ether was removed by rotary evaporation.

The crude product was then subjected to kugelrohr distillation at 2 mmHg. One fraction was isolated as a thick clear colourless oil (1.70 g, 64 %) at 130-150°C Lit.[16] 131°C at 3 mmHg.

Diborane facilitated reduction.

The reduction procedure described in Section 3.10.4 was followed and the following amounts were used- boron trifluoride diethyl etherate (1.59 mL, 10.0 mmol), dry THF (50 mL), $NaBH_4$ (0.904 g, 23.9 mmol) and 3,3-dimethylglutaric acid (1.10 g, 6.85 mmol). Reduced pressure distillation (130-140°C at 2mmHg) was used to isolate the desired diol (0.875 g, 97 %) as a thick clear colourless oil. Lit.[16] 131°C at 3 mmHg.

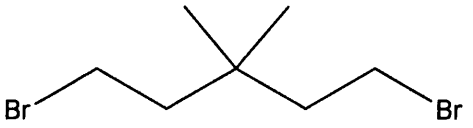


^{1}H-NMR ($CDCl_3$) δ 0.98 (6H, s, 2 x CH_3), 1.62 (4H, t, J = 7 Hz, 2 x $CH_2C(CH_3)_2$), 2.90 (2H, s, OH, D_2O exchangeable) 3.50 (4H, t, J = 7 Hz, 2 x $HOCH_2$). ^{13}C-NMR ($CDCl_3$) δ 28.6 (CH_3), 32.0 (C), 44.3 (CH_2), 59.7 ($HOCH_2$). FTIR (neat) *v* 3307 (OH *str*), 1031, 1008 (C-O *str* and O-H *def*). MS ES$^-$ m/z 131 ([M-H]$^-$, 80 %), 113 ([M-H-H_2O]$^-$ 100 %]). HRMS CI$^+$(NH_3) m/z calcd for $[M+NH_4]^+$ 150.1489, found 150.1488.

3.10.12 Synthesis of 1,5-dibromo-3,3-dimethylpentane.

The method described in Section 3.10.5 was followed and the following amounts were used- HBr (4.21 mL, 25 mmol, 48 %), concentrated sulfuric acid

(4.89 g, 50 mmol), 3,3-dimethyl-1,5-pentandiol (1.65 g, 12.5 mmol). After aqueous work up the crude oil (1.62 g) was subjected to reduced pressure distillation at 6 mmHg. One fraction (140-155 °C) was obtained as a clear colourless oil (1.36 g, 41 %). Lit.[16] 93-98°C at 3 mmHg.



^{1}H-NMR ($CDCl_3$) δ 0.98 (6H, s, 2 x CH_3), 1.92 (4H, t, J = 7 Hz, $CH_2C(CH_3)_2$), 3.50 (4H, t, J = 7 Hz, 2 x $BrCH_2$).^{13}C-NMR ($CDCl_3$) δ 26.9 (CH_2), 28.9 (CH_3), 36.1 (C), 45.7 ($BrCH_2$). FTIR (neat) *v* 666 (C-Br *str*). MS EI$^+$ m/z 260 ([M(2 x ^{81}Br)]$^+$, 50 %), 258 ([M(^{81}Br,^{79}Br)]$^+$, 100 %), 256 ([M (2 x ^{79}Br)]$^+$, 50 %). HRMS EI$^+$ m/z calcd for [M (2 x^{79}Br)]$^+$ 255.9457, found. 255.9455.

3.10.13 Synthesis of 1,5-dibromo-3,3-dimethylpentane by sequential reduction-substitution of 3,3-dimethylglutaric acid.

Boron trifluoride diethyl etherate (1.59 mL, 10.0 mmol), in dry THF (50 mL) was added slowly to an oven dried 100 mL round bottomed flask containing 3,3-dimethylglutaric acid (1.10 g, 6.85 mmol), $NaBH_4$ (0.904 g, 23.9 mmol) and dry THF (50 mL).

The mixture was then refluxed and the reaction was followed by thin layer chromatography until all the starting material was consumed. This took approximately 5 h. The vessel was allowed to cool and was then quenched with water (25 mL). The solvents (including water) were then removed by rotary evaporation giving rise to a white precipitate which was assumed to contain the desired diol and inorganic by-products. In a separate 10 mL round bottomed flask fitted with a reflux condenser was placed hydrobromic acid (0.75 mL, 13.7 mmol, 48 %). The flask was cooled by an external ice bath. Concentrated sulfuric acid (1.46 mL, 27.4 mmol) was added cautiously in drop-wise manner to the hydrobromic acid. The HBr acid mixture was then pipetted slowly onto the diol containing mixture. The reaction was left to stir overnight, then was heated on a water bath for 3 h before being left to cool. The

organic components were extracted with dichloromethane (15 mL x 2). The organic phases were combined and washed with water (30 mL), 10 % Na_2CO_3 (30 mL), and then dried over $MgSO_4$. The drying agent was filtered off and the solvents were removed by rotary evaporation, to give a brown coloured crude oil (1.22 g). Column chromatography using hexane as the eluent and silica as the stationary phase was undertaken. One fraction (1.12 g, 63 %) was isolated as a clear oil. The characteristics of the product were identical to those described above (see Section 3.10.12).

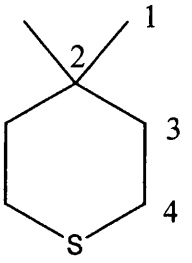
3.10.14 Attempted synthesis of Polymer 8 from 1,5-dibromo-3,3-dimethylpentane.

1,5-Pentanedithiol (0.78 ml, 5.8 mmol) and dry THF (10 mL) were placed into a dry 100 mL round bottomed flask which was flushed with N_2. The flask was cooled to -78°C using dry ice and acetone. Butyllithium (2.5M, 4.65 mL, 11.6 mmol) was added slowly over 20 minutes. The reaction mixture was allowed to proceed for 30 minutes, and the mixture was then allowed to warm to room temperature. 1,5-Dibromo-3,3-dimethylpentane (1.35 g, 5.23 mmol) was added *via* a dry syringe and the reaction was left to proceed for 1 h. 1-Bromobutane (0.16 g, 1.16 mmol) was then added and the reaction was left to proceed for 18 h. The reaction was quenched with water (20 mL). No insoluble precipitate was present. Dichloromethane (20 mL) was added and extraction was undertaken. The aqueous phase was re-extracted 5 times with dichloromethane (5 x 15 mL). The organic phases were combined and dried over $MgSO_4$. The drying agent was then filtered off. The solvent was removed by rotary evaporation to give a crude oil. Any remaining volatile material was removed under reduced pressure in a vacuum oven (100°C, 2mmHg) to leave the residue (0.92 g). H^1NMR integrals were not as expected for the desired polymer. The integration probably represented a mixture of oligomers (see Section 3.5.4).

3.10.15 Synthesis of 4,4-dimethyltetrahyrdrothiopyran.

The standard Method B conditions were applied and the amounts used were as follows: 1,5-dibromo-3,3-dimethylpentane (1.00 g, 3.87 mmol), $Na_2S.9H_2O$ (1.40 g, 5.81 mmol). The organic material was extracted into dichloromethane (25 mL) and was then washed with water (25 mL), saturated aqueous NH_4Cl (25 mL) and then

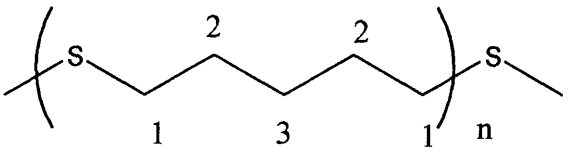
brine (25 mL). The organic phase was dried over $MgSO_4$. The drying agent was then filtered off. The solution was subjected to reduced pressure distillation at 20 mmHg of pressure. The dichloromethane was first removed and then the 4,4-dimethyltetrahydrothiopyran (0.261 g, 58 %) was collected as a clear colourless oil at 60-65 °C. Lit.[17] 57-58°C at 15 mmHg. Some 1,5-dibromo-3,3-dimethylpentane starting material was then distilled from the residue at 85°C at 2 mmHg pressure (0.040 g, 4 %).



^{1}H-NMR ($CDCl_3$) δ 0.75 (6H, s, 2 x CH_3), 1.40-1.60 (4H, m, $C3H_2$), 2.50-2.60 (4H, m, CH_2S). ^{13}C-NMR ($CDCl_3$) δ 24.8 (C4), 26.9 (C1), 28.8 (C2), 40.2 (C3). FTIR (neat) ν 648 (possibly C-S str). MS EI$^+$ m/z 130 ($[M]^+$, 90 %), 115 ([M-CH_3], 95 %), 69 ($C_5H_9^+$, 70 %), 41 ($C_3H_5^+$, 80 %).

3.10.16 Synthesis of poly(sulfanediylpropane-1,5-diyl) (Polymer 5-5).

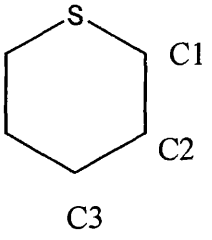
Method A was applied and the following amounts were used: 1,5-pentanedithiol (2.00 ml, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), 1,5-dibromopentane (3.10 g, 13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). The crude white powder obtained after the filtration and washing steps was then removed from any volatile components by heating to 50°C at 2 mmHg for 4 h to give the final white powder product (2.36 g, 77 %).



^{1}H-NMR ($CDCl_3$) δ 1.45 (2H, q, J = 6.5, $CH_2CH_2CH_2$), 1.60 (4H, m, SCH_2CH_2), 2.45 (4H, t, J = 6 Hz, SCH_2). ^{13}C-NMR ($CDCl_3$) δ 29.2 ($CH_2CH_2CH_2$), 29.7 (SCH_2CH_2), 32.4 (SCH_2). FTIR (neat) *v* 723 (possibly C-S str). GPC M_n 6160.

3.10.17 Synthesis of tetrahydrothiopyran.

Standard Method A conditions were applied and the following amounts were used: 1,5-dibromopentane (4.0 g, 17.4 mmol) and sodium sulfide nonahydrate (6.27 g, 26.1 mmol). The crude oil obtained after aqueous work up was then subjected to reduced pressure distillation (15 mmHg). One fraction was obtained at 50-55°C as a colourless oil (1.60 g, 80 %). Lit.[18] 138-140°C at ambient pressure.

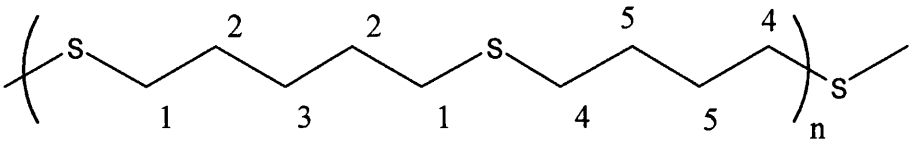


^{1}H-NMR ($CDCl_3$) δ 1.55-1.65 (2H, m, $C3H_2$), 1.80-1.90 (4H, m, $C2H_2$) , 2.60-2.70 (4H, m, SCH_2). ^{13}C-NMR ($CDCl_3$) δ 26.8 (C3), 28.1 (C2), 29.4 (C1). FTIR (neat) *v* 655 (possibly C-S str). MS EI$^+$ m/z 102 ($[M]^+$ 100 %), 87 ($[C_4H_7S]^+$, 95 %), 67 (60 %), 46 ($[SCH_2]^+$ 75 %), 39 (80 %).

3.10.18 Synthesis of poly(sulfanediylbutane-1,4-diylsulfanediylpropane-1,5-diyl) (Polymer 5-4)

Method A was applied and the following amounts were used: 1,5-pentanedithiol (2.00 ml, 15 mmol), dry THF (20 mL) butyllithium (2.5M, 12.0 mL, 30 mmol) 1,4-dibromobutane (2.915 g ,13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). After filtration and washing the crude powder was then removed

from any volatile components by heating to 50°C at 2mmHg for 4 h. The resulting white powder product was obtained (2.24 g, 79 %).

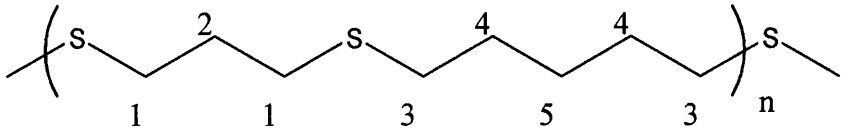


^{1}H-NMR ($CDCl_3$) δ 1.30-1.80 (10H, m, CH_2), 2.30-2.60 (8H, appt. t, J = 7.5 Hz, CH_2S). ^{13}C-NMR ($CDCl_3$) δ 28.6, 29.1, 29.7 (C2, C3, C5) 32.1, 32.4 (C4, C1). FTIR (neat) *v* 728 (possibly C-S str). GPC M_n 6390.

3.10.19 Synthesis of poly(sulfanediylpropane-1,3-diylsulfanediylpentane-1,5-diyl) (polymer 5-3).

Method A was applied and the following amounts were used: 1,5-pentanedithiol (2.00 ml, 15 mmol), dry THF (20 mL) butyllithium (2.5M, 12 mL, 30 mmol), 1,3-dibromobutane (2.72 g ,13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). After filtration and washing the crude powder was then removed from any volatile components by heating to 50°C at 2 mmHg for 4 h. The resulting white powder was obtained (2.06 g, 78.0 %).

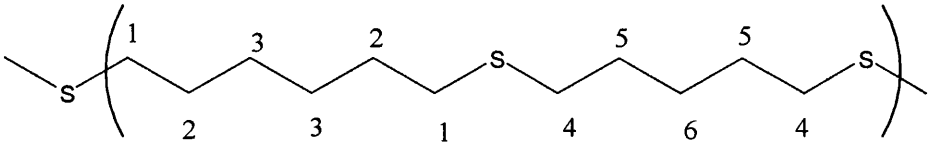
^{1}H-NMR ($CDCl_3$) δ 1.30-1.60 (6H, m, CH_2, *pentylene*), 1.60-1.90 (2H, q, J = 7 Hz, $SCH_2C\mathit{H}_2CH_2S$), 2.45 (4H, t, J = 7 Hz, CH_2S *pentylene*) 2.58 (4H, t, J = 7 Hz, CH_2S *propylene*).



^{13}C-NMR ($CDCl_3$) δ 28.5, 29.7, 29.8 (C2, C4, C5), 31.3, 32.4 (C3, C1). FTIR (neat) *v* 730 (possibly C-S str).GPC M_n 7250.

3.10.20 Synthesis of poly(sulfanediylpropane-1,5-diylsulfanediylhexane-1,6-diyl) (Polymer 5-6).

Method A was applied and the following amounts were used: 1,5-pentanedithiol (2.00 ml, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12.0 mL, 30 mmol), 1,6-dibromohexane (3.29 g, 2.10 mL, 13.5 mmol) and 1-bromobutane (0.41 g, 3 mmol). The crude powder isolated after filtration and washing was removed from any volatile components by heating to 60°C at 5 mmHg for 4 h. During the drying stage the white powder partially melted and re-solidified to form a grey glass-like material. The grey material was dissolved in a minimum amount of dichloromethane and re-precipitated by the addition of excess methanol. The resulting white powder was collected by Buchner filtration and dried at 50°C at 5mmHg for 4 h to give the resulting white powder (2.13 g, 65 %).



^{1}H-NMR ($CDCl_3$) δ 1.30-1.80 (14H, m, CH_2), 2.30-2.60 (8H, appt. t, J = 7 Hz, CH_2S). ^{13}C-NMR ($CDCl_3$) δ 28.4, 28.6, 29.5, 29.7 (C2, C3, C5, C6), 32.4, 32.5 (C4, C1). FTIR (neat) *v* 726 (possibly C-S str). GPC M_n 6840.

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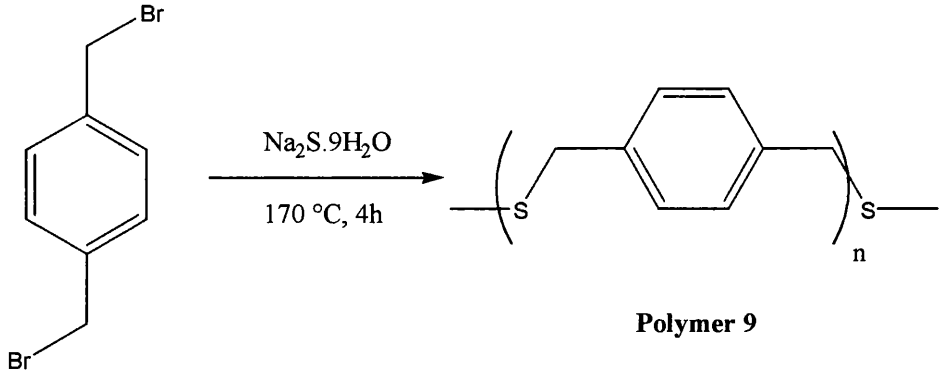
Chapter 4: Syntheses of aromatic and cyclic aliphatic ring containing thiapolymers and their use as catalysts for the chlorination of phenols.

4.1 Synthesis of novel aromatic ring containing thiapolymers.

This chapter reports the continuation of the synthesis of novel thiapolymers for the use as potential selective catalysts for the chlorination of phenols and involves the synthesis of thiapolymers containing aliphatic and aromatic rings. As previously mentioned diphenyl sulfide[1] has been used as a selective catalyst for the chlorination of phenols. The polymeric analogue of diphenyl sulfide (polyphenylsulfide, PPS) has also been tested as a catalyst for the chlorination of phenols[1,2] and performs moderately. The syntheses of more aromatic containing thiaalkanes are reported in this chapter. These polymers will intrinsically possess different electronic and steric properties to their aliphatic analogues. The aromatic ring is planar and rigid and this will affect the way the polymer exists in solution, *i.e.* the way it folds upon itself, which in turn will affect the nature and accessibility of the catalytic sulfur atoms.

4.1.1 Synthesis of Polymer 9 from α, α'-dibromo-*p*-xylene by synthetic Method B.

The commercially available α,α'-dibromo-*p*-xylene(**101**) was reacted under the standard Method B procedure (Scheme 4.1).



101 **Polymer 9**

Scheme 4.1: Synthesis of **Polymer 9** by the standard Method B polymer conditions using α,α'-dibromo-*p*-xylene (**101**).

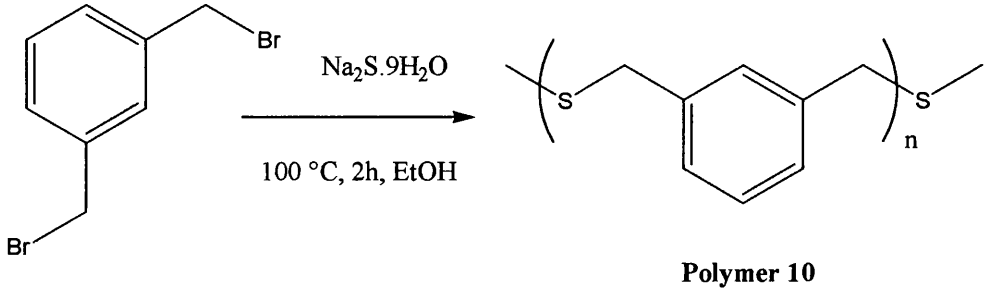
The reaction was allowed to proceed for 4 hours. Within one hour a white/yellow precipitate formed. This product was isolated by suction filtration and was then washed with a series of solvents. The resulting powder product proved to be insoluble in dichloromethane, chloroform, DMSO, DMF, and trifluoroacetic acid and therefore no NMR or GPC analysis has been carried out. FTIR analysis of the dibromide starting material and that of the product showed differences in the characteristic absorptions of *para*-substituted benzene species. In the product the C-Br band at 608 cm^{-1} was no longer observed and a new band at around 700 cm^{-1} was observed, which is likely to be due to a C-S stretch.[3]

4.1.2 Synthesis of Polymer 10 from α,α'-dibromo-*m*-xylene by synthetic Method B.

The standard Method B conditions used above were next applied to α,α'-dibromo-*m*-xylene (**102**). The reaction proceeded to give a highly insoluble plastic-like material. After stirring in the presence of dichloromethane for several days the hard plastic material turned into a more manageable powder like material.

The rate of the polymerization in this reaction appears to be very high as the insoluble polymeric material appeared to form within the first hour of the reaction. The relatively quick progression of the polymerization is probably due to the reaction proceeding *via* a stable benzylic cation intermediate.

In a bid to slow the reaction down and obtain a less insoluble/ less plastic like product, milder reaction conditions (ethanol reflux for 2 hours) were then applied for the synthesis of **Polymer 10** (Scheme 4.2).



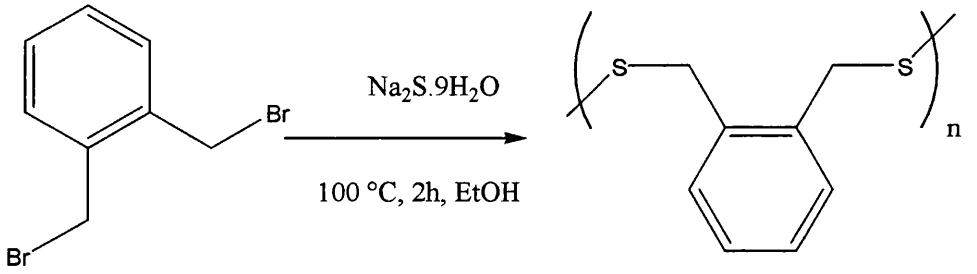
102 **Polymer 10**

Scheme 4.2: Synthesis of **Polymer 10** by the reaction of α,α'-dibromo-*m*-xylene (**102**) under a milder ethanolic reflux adaptation of Method B .

The α α'-dibromo-*m*-xylene (**102**) in the presence of 1.5 mole equivalents of sodium sulfide was refluxed in ethanol for 2 hours. The reaction was successful in giving a more powder-like material. However, the product of this reaction was equally as insoluble as the former. FTIR spectroscopy was utilised to confirm that the expected polymerization had probably occurred during these two reactions and it was observed that from starting material to product there was a loss of a band at around 570 cm^{-1} (C-Br) and an appearance of two new bands at 705 and 693 cm^{-1}, one of which is probably due to a C-S stretch and the other due to a C-H wag (*meta*). The two products isolated from the two different reaction conditions gave practically identical infrared spectra. It is possible however that these two products may differ in some way that is not observed by standard FTIR analysis. For example, the two polymers may have different molecular weights and therefore both of the products were tested as catalysts. It is highly likely that the plastic like material obtained from the standard Method B conditions possesses a higher molecular weight to the powder material obtained under the milder ethanol reflux conditions.

4.1.3 Attempted synthesis of Polymer 11 from α,α'-dibromo-*o*-xylene by synthetic Method B.

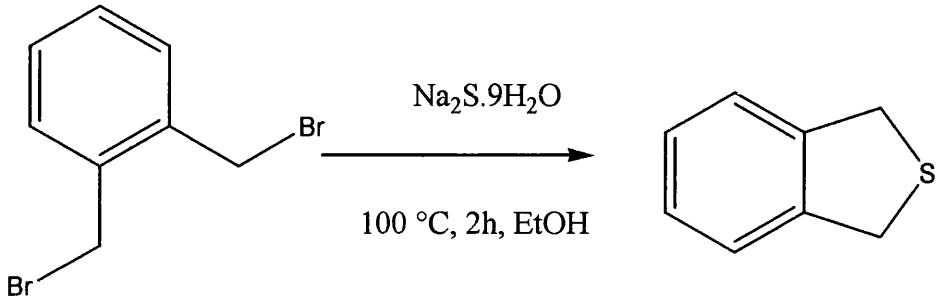
The 2 hour ethanol reflux conditions were next applied to α,α'-dibromo-*o*-xylene (**103**) with the intention of synthesising the analogous *ortho* substituted thiapolymer (**Polymer 11**, Scheme 4.3).



103 **Polymer 11**

Scheme 4.3: Attempted synthesis of **Polymer 11** by the reaction of α,α'-dibromo-*o*-xylene (**103**) with sodium sulfide in refluxing ethanol.

However, during the progression of this reaction no insoluble precipitate formed, unlike in the analogous polymer forming reactions reported above. Also, no precipitate formed during the quenching of the reaction. Dichloromethane and water were added to the reaction vessel and then extraction was undertaken. TLC analysis of the dichloromethane solution suggested that there was one main reaction product and that the starting material was completely consumed. Also, the organic phase had a distinct sulfurous smell. It was speculated that although polymerization did not seem to have occurred there had been a clean reaction. It was speculated that due to the close proximity of the bromide groups on the *ortho* benzyl carbons then the intramolecular reaction (see Section 3.7) was once again favoured (Scheme 4.4).



103 **104**

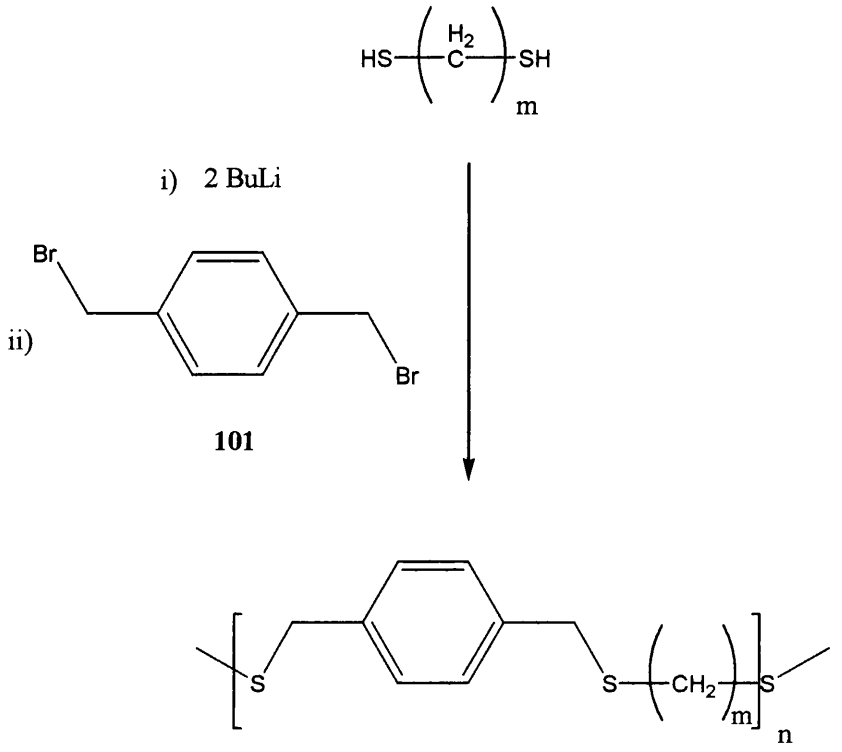
Scheme 4.4: Synthesis of a 1,3-dihydrobenzo[*c*]thiophene (**104**) from α, α'-dibromo-*o*-xylene (**103**) by the reaction with sodium sulfide in refluxing ethanol.

After aqueous workup the crude product was subjected to reduced pressure distillation at 6mmHg at 90 °C, and one component was isolated (68 %) as a clear colourless liquid and confirmed as the expected 1,3-dihydrobenzo[*c*]thiophene (**104**).

4.1.4 Synthesis of semi-aromatic thiapolymers.

As previously stated the incorporation of the rigid aromatic ring will affect the flexibility of the polymer and therefore its ability and tendency to fold up upon itself. By using a combination of aliphatic and aromatic components the degree of flexibility in the polymer can be controlled and by increasing the length of the aliphatic component in the repeating unit a polymer with distinctly different levels of rigidity can be obtained.

The polymer forming Method A was utilised to react α,α'-dibromo-*p*-xylene (**101**) with a series of aliphatic dithiolates of various lengths (Scheme 4.5).



Where m=2,3,4,5,6,8,10

Scheme 4.5: Method A syntheses of various semi aromatic polythiaalkanes by the reaction of various linear dithiols with α,α'-dibromo-*p*-xylene (**101**).

Table 4.1: Syntheses of semi aromatic polymers by Method A according to Scheme 4.5.[a]

m	Yield mol%	Solubility in $CDCl_3$	M_n[b]
2	62	Insoluble	-
3	55	Soluble	4780
4	56	Insoluble	-
5	69	Soluble	3790
6	65	Poor	-
8	52	Insoluble	-
10	52	Soluble	4710

[a]The standard Method A conditions were applied to various linear dithiols and the resulting dithiolates were reacted with α,α'-dibromo-*p*-xylene (**101**). See Scheme 4.5.

[b] As determined by GPC. Only obtainable for the soluble materials.

Table 4.1 shows that all the reactions proceeded in moderate yield (52-69 %). These polymers gave an unexpected pattern of solubility in $CDCl_3$. In the first consideration it may be assumed that the more aliphatic the polymer becomes then the more it may be solvated by $CDCl_3$ by favourable van der Waals interactions at the aliphatic regions. Also, the more flexible the polymer becomes then the more likely it is to exist in an irregular grouping of polymer chains with relatively less favourable van der Waals forces between different polymer chains. The inter molecular forces between solvent and polymer may therefore be more feasible than between polymer and polymer. It may be expected that the shorter and more rigid polymer strands are more likely to interact more strongly and more regularly with each other and therefore be less exposed to the solvent and therefore less soluble. However, these considerations do not match the observed pattern of solubility.

It is conceivable that the solubility is actually determined by the length of the polymer chains that exist, due to a greater sum of van der Waals interactions that can then exist, in the same way that linear alkanes become less soluble the more carbon atoms they contain. However, this speculation could not be investigated as the polymers that showed poor solubility or insolubility were unable to be analysed by GPC.

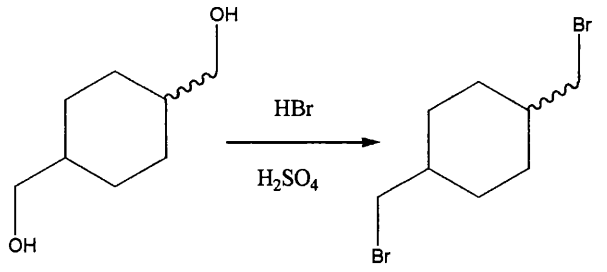
4.2 Syntheses of some cyclic aliphatic ring containing thiapolymers.

In order to continue the syntheses of novel thiapolymers and to investigate the effect different types of thiapolymers have on the selectivity of chlorination it was decided that the syntheses of cyclic aliphatic containing thiapolymers would be undertaken.

It would be expected that the cyclic aliphatic containing polymers would be intrinsically more flexible than their aromatic equivalent and bulkier than their linear aliphatic analogous.

4.2.1 Synthesis of 1,4-bis(bromomethyl)cyclohexane

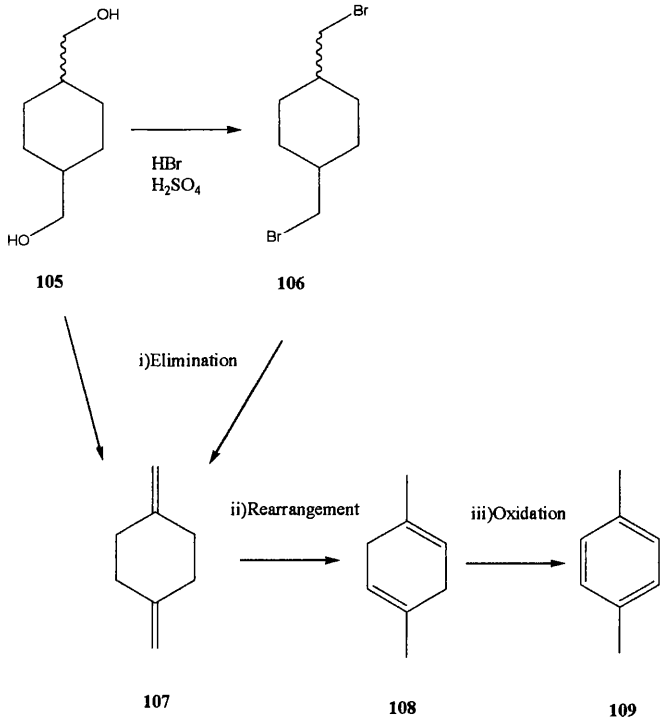
A mixture of *cis*- and *trans*-4-(hydroxymethyl)cyclohexylmethanol (**105**) is commercially available and was refluxed in hydrobromic acid in the presence of concentrated sulfuric acid in order to obtain the equivalent dibromo compound (**106,** Scheme 4.6) required for the synthesis of the thiapolymer.



105 **106**

Scheme 4.6: Hydrobromic acid substitution of 4-(hydroxymethyl)cyclohexylmethanol (**105**) to form 1,4-bis(bromomethyl)cyclohexane (**106**) .

After aqueous work up the crude oil was subjected to reduced pressure distillation in the hope of isolating the desired dibromo compound (**106**). However, during distillation a slow but continuous amount of lower boiling compounds were distilled until only a thick black residue remained. NMR analysis was used to show that the lower boiling fraction was a mixture containing primarily *p*-xylene (**109**) with some 1-bromomethyl-4-methylbenzene (**110,** Scheme 4.8) and that the higher boiling fractions contained the desired dibromocyclohexane (**106**) but with persistent impurities of the aromatic by-products. The proposed reaction pathway is illustrated in Scheme 4.7.



105 **106** **107** **108** **109**

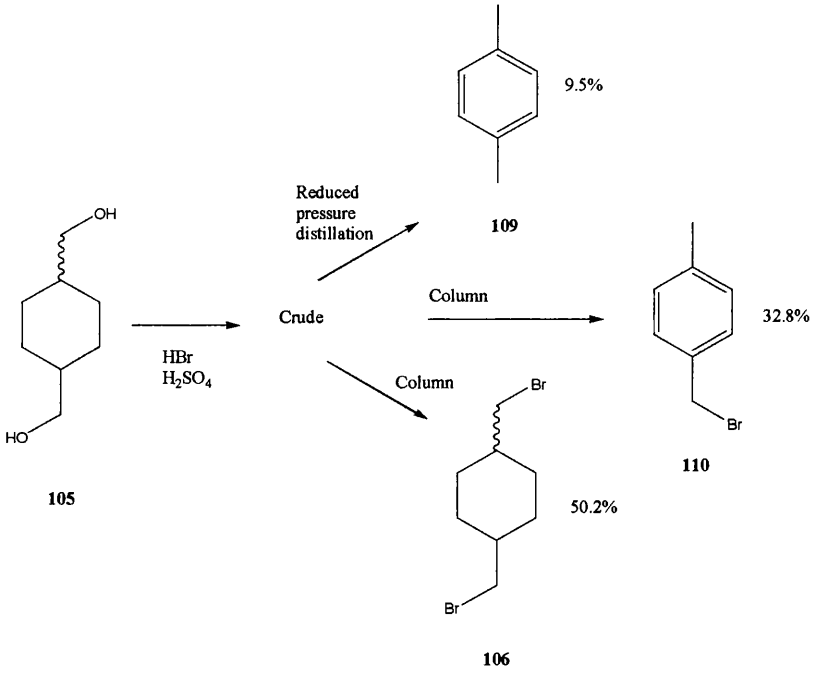
Scheme 4.7: Side reaction of the hydrobromic acid substitution of

4-(hydroxymethyl)cyclohexylmethanol (**105**); formation of *p*-xylene (**109**).

The initial step is likely to be the formation of a diene (**107**) by double elimination. In general the hydroxyl group is less susceptible to elimination than a bromide and therefore it is likely that the latter is the major precursor to the cyclohexadiene. However, primary alcohols are susceptible to elimination in the presence of sulfuric acid.[4]

The second step is a simple rearrangement to the more stable diene (**108**). The final step is an oxidation to the aromatic compound (**109**). The conversion of cyclohexadienes to aromatic compounds is fairly common[5] and is likely to be promoted by the oxidising sulfuric acid that is present.

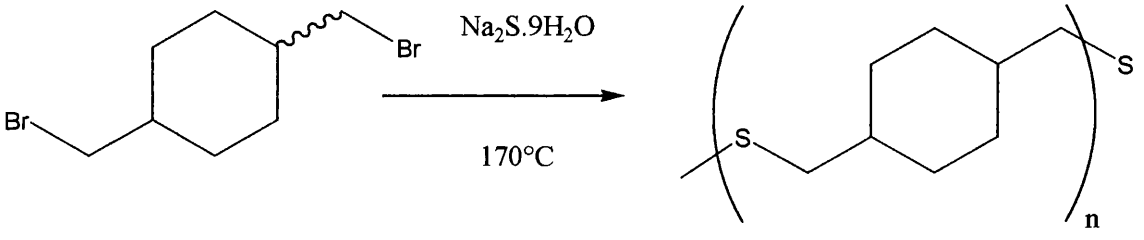
Considering the distillation took place very slowly over several hours then it is very likely that the elimination, rearrangement and oxidation were occurring to some extent under the applied heat of the distillation. Therefore, the isolated mixture was not a true representation of the actual reaction products. In order to determine the actual products the reaction was repeated. This time more caution was taken during the isolation, and the *p*-xylene (**109**) was removed under low heat and pressure. The remaining crude product was subjected to column chromatography (Scheme 4.8).



Scheme 4.8: Formation and isolation of *p*-xylene (**109**), 1-bromomethyl-4-methylbenzene (**110**) and 1,4-bis(bromomethyl)cyclohexane (**106**) from the hydrobromic acid substitution of (4-hydroxycyclohexyl)methanol (**105**).

The two components isolated from the column proved to be 1-bromomethyl-4-methylbenzene (**110**) and the desired 1,4-bis(bromomethyl)cyclohexane (**106**). However, NMR analysis of both of these fractions indicated the presence of impurities. The 1,4-bis(bromomethyl)cyclohexane was not subjected to any further purification steps as it was deemed appropriate to investigate an alternative method to synthesise the dibromocyclohexane in a cleaner fashion and also to isolate it in a less tedious manner. The establishment of a better alternative route was important, as the method would also be utilised for analogous reactions using the equivalent 1,3- and 1,2-disubstituted cyclohexanes.

Despite the presence of impurities the dibromoalkane (**106**) isolated from this reaction was used in a test polymer forming reaction (Scheme 4.8) in order to ascertain the degree of reactivity of these compounds with sodium sulfide and to assess the feasibility of polymer formation.



106 **Polymer 12**

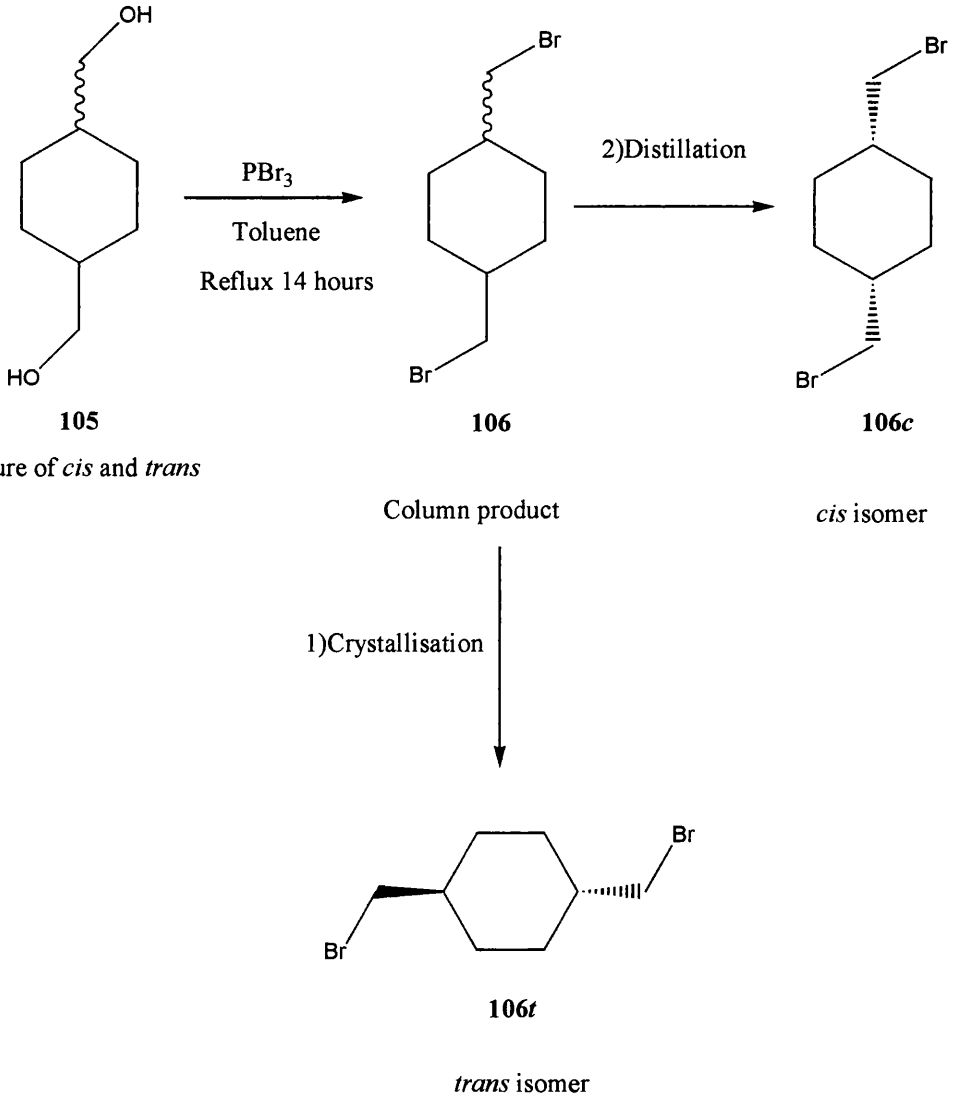
Scheme 4.8: Synthesis of **Polymer 12** from 1,4-bis(bromomethyl)cyclohexane (**106**).

The standard Method B reaction was applied to the impure mixture of *cis* and *trans* 1,4-bis(bromomethyl)cyclohexane (**106**) and the reaction was allowed to proceed for 6 hours. No insoluble product was observed. Dichloromethane was added and aqueous extractions were undertaken. The eventual crude oil obtained was analysed by NMR, which showed that 66 % of the original CH_2Br groups remained and therefore only 34 % of the desired CH_2S groups had formed. Ignoring the complication presented due to the small amounts of impurities it can be concluded that the polymer forming step progresses considerably slower than when the linear aliphatic bromides were used, presumably due to the bulkier ring introducing a significant steric effect making the reactive groups less likely to interact. Also, the

reaction is significantly slower than when the equivalent benzylic dibromides are used, presumably because the ease of formation of the benzylic carbocations induces a change in mechanism to S_N1, whereas the aliphatic dibromides proceed via an S_N2 mechanism.

4.2.2 Alternative route to 1,4-bis(bromomethyl)cyclohexane.

Phosphorus tribromide was used for the substitution (Scheme 4.9) and was chosen because it is not a strong eliminating or oxidising agent, unlike the sulfuric acid/hydrobromic acid mixture previously used.



105

Mixture of *cis* and *trans*

106

Column product

106*c*

cis isomer

106*t*

trans isomer

Scheme 4.9: Isolation of *cis*- and *trans*-1,4-bis(bromomethyl)cyclohexane (**106*c***, **106*t***) from the phosphorus tribromide substitution of 4-(hydroxymethyl)cyclohexyl methanol (**105**).

The crude product of the reaction was initially passed through a silica column in order to remove any starting material (**105**) or hydroxyl group containing intermediates. As indicated by Scheme 4.9 the crude column product was a mixture of the *cis*- and *trans*-isomers (**106*c*** and **106*t***). Upon standing the *trans*-isomer crystallised out from the *cis*-isomer. The *trans*- isomer was then re-crystallised from hot toluene. The *cis*-isomer was isolated by reduced pressure fractional distillation. The physical properties and the NMR analysis of these components confirmed them as the *cis*- and *trans*- products. No aromatic products were observed. To obtain more product for the next synthetic steps the reaction was conducted twice and the results are reported in the Table 4.2.

Table 4.2: Yields of *cis*- and *trans*-1,4-bis(bromomethyl)cyclohexane (**106*c*** and **106*t***) isolated from the phosphorus tribromide substitution of 4-(hydroxymethyl)cyclohexylmethanol (**105**).[a]

106*t* / mol%[b]	**106*c*** / mol%[c]	Overall yield/ %
33.8	11.9	45.7
27.3	10.1	38.4

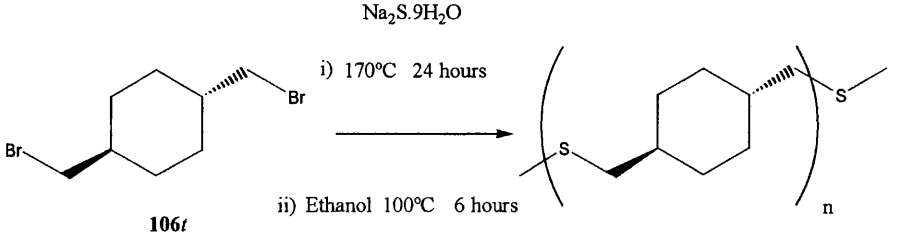
[a] A mixture of *cis*- and *trans*-4-(hydroxymethyl)cyclohexylmethanol (35 mmol) was refluxed in dry toluene overnight in the presence of PBr_3 (35 mmol). See Scheme 4.5.

[b]Isolated yield after recrystallisation.

[c]Isolated yield after reduced pressure fractional distillation.

4.2.3 Synthesis of Polymers 12a and 12b from *trans*- and *cis*-1,4-bis(bromomethyl)cyclohexane.

The *trans*-product (**106*t***) was then reacted with sodium sulfide in a bid to synthesise **Polymer 12a** (Scheme 4.10).



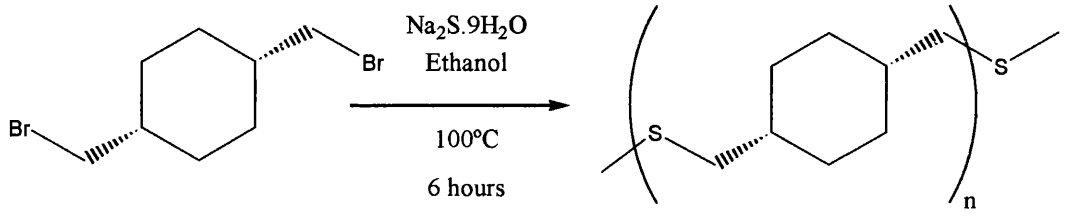
106*t*

Polymer 12a

Scheme 4.10: Synthesis of **Polymer 12a** by the reaction of *trans*-1,4-bis(bromomethyl)cyclohexane (**106*t***) with sodium sulfide.

Following the incomplete reaction after 6 hours when the impure mixture of *cis*- and *trans*-1,4-bisbromomethylcyclohexane (**106**) was used (see Section 4.2.1) the solvent free reaction with sodium sulfide was heated to 170 °C and allowed to proceed for 24 hours. ^{1}HNMR analysis of the isolated product showed that there was only 6 % remaining CH_2Br groups relative to the newly formed CH_2S groups. An ethanolic reflux was then undertaken and the reaction proceeded even more extensively to leave around only 4 % of the CH_2Br groups. The M_n of the latter polymer was determined to be 705 by GPC.

The successful ethanol reflux conditions were next applied to the *cis*-1,4-bis(bromomethyl)cyclohexane (**106*c***, Scheme 4.11).



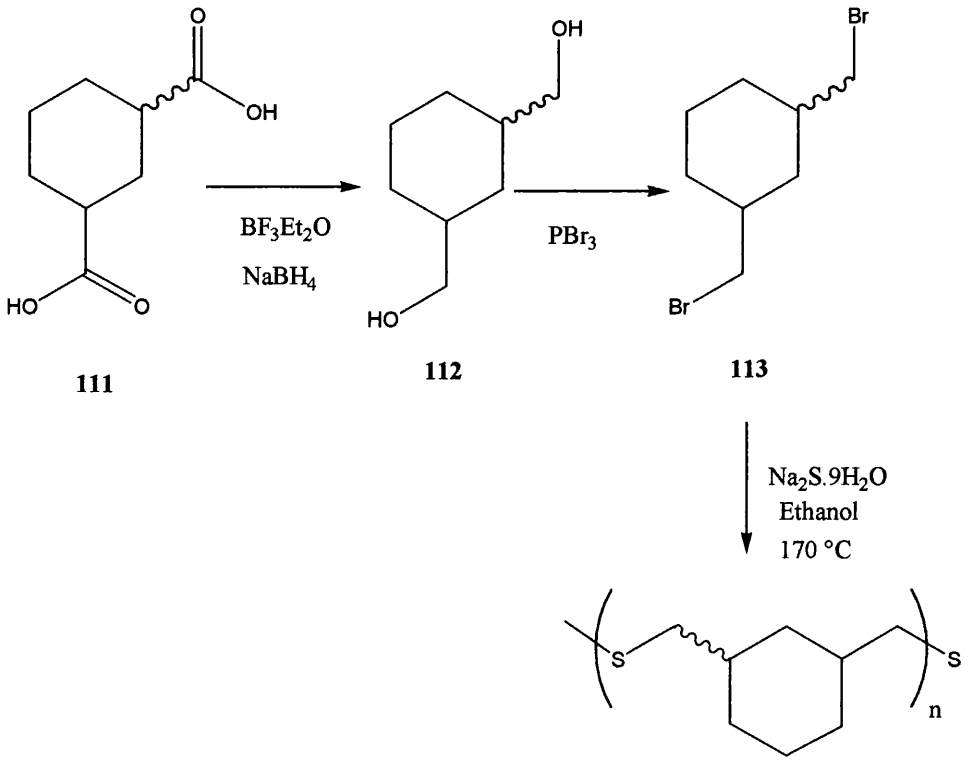
106*c* **Polymer 12b**

Scheme 4.11: Synthesis of **Polymer 12b** from *cis*-1,4-bis(bromomethyl)cyclohexane (**106*c***)

The polymerization also proceeded successfully for the *cis*- isomer (**106*c***) leaving only 2 % of the remaining CH_2Br groups. The M_n of this polymer was determined to be 810 by GPC.

4.2.4 Synthesis of Polymer 13 from 1,3-(bisbromomethyl)cyclohexane.

The synthesis of an analogous polymer from 1,3-bis(bromomethyl)cyclohexane (**113**) was next proposed. However, **113** is not commercially available and therefore required synthesis. A synthetic route to this compound from the commercially available dicarboxylic acid (**111**) is shown in Scheme 4.12.



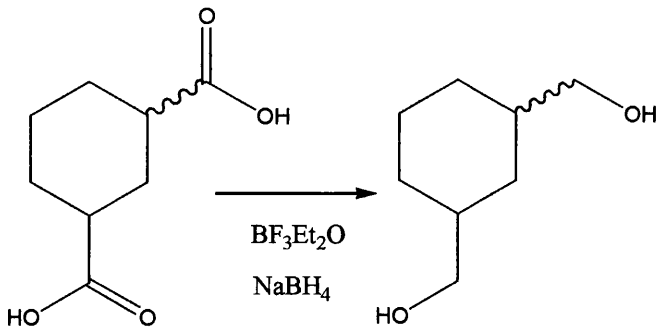
Polymer 13

Scheme 4.12: Proposed synthetic route to **Polymer 13** by the reduction of cyclohexane-1,3-dicarboxylic acid (**111**) to 3-(hydroxymethyl)cyclohexylmethanol (**112**) followed by substitution by PBr_3 to form 1,3-(bisbromomethyl)cyclohexane (**113**) required for the Method B polymer forming step.

The diborane reduction method that was utilised for the quantitative reduction of glutaric acids to pentane-1,5-diols as reported in chapter 3 was proposed for the reduction of the commercially available cyclohexane-1,3-dicarboxylic acid (**111**). The phosphorus tribromide substitution was proposed for the substitution step as it was successful for the synthesis of 1,4-bis(bromomethyl)cylohexane (**106**, see Section 4.2.2) from the equivalent diol (**105**) without the generation of any unwanted aromatic by-products.

4.2.4.1 Synthesis of 3-(hydroxymethyl)cyclohexylmethanol.

The standard conditions used previously for the diborane reduction (see Section 3.10.4) were used on the commercially available mixture of *cis*- and *trans*-cyclohexane-1,3-dicarboxylic acids (**111**, Scheme 4.13).



111 **112**

Scheme 4.13: Diborane reduction of cyclohexane-1,3-dicarboxylic (**111**) acid to 3-(hydroxymethyl)cyclohexylmethanol (**112**).

The diborane reduction once again proceeded in a quantitative fashion with excellent isolated yields. The reaction was conducted initially on a trial scale and secondly on a larger scale and the results are shown in Table 4.3.

Table 4.3: Product yields of the reduction of cyclohexane-1,3-dicarboxylic acid (**111**).[a]

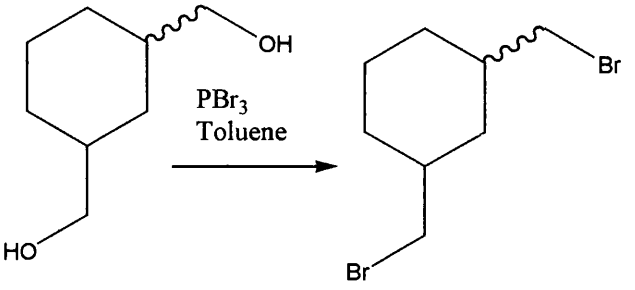
Reaction scale, mmol of cyclohexane-1,3-dicarboxylic acid	Yield of **112**/ mol %[b]	Appearance
5.1	96.7	Clear colourless oil
25.5	96.8	Clear colourless oil

[a]Cyclohexane-1,3-dicarboxyclic acid was refluxed in dry THF in the presence of BF_3Et_2O and $NaBH_4$ for 6 h. See Scheme 4.13.

[b] Isolated yield after reduced pressure distillation.

4.2.4.2 Synthesis of 1,3-bis(bromomethyl)cyclohexane.

The mixture of *cis*- and *trans*-3-(hydroxymethyl)cyclohexylmethanol (**112**) isolated from the reduction step was used in the next synthetic step; the phosphorus tribromide substitution step (Scheme 4.14).



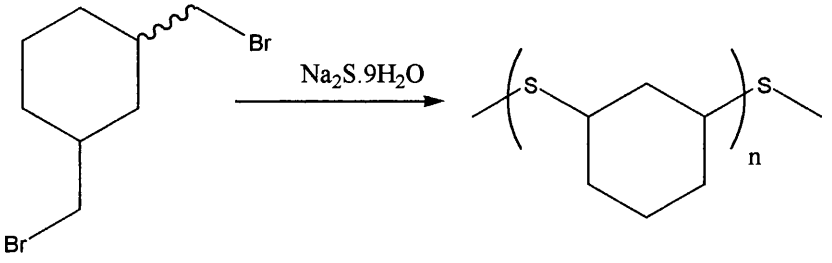
112 **113**

Scheme 4.14: Phosphorus tribromide substitution of 3-(hydroxymethyl)cyclohexylmethanol (**112**) to form 1,3-(bisbromomethyl)cyclohexane (**113**)

Identical conditions used for the equivalent 1,4-disubsituted diol (**105**, see Section 4.2.2) was utilised and 48 % of the desired product (**113**) was obtained after the application of both column chromatography and reduced pressure distillation. Upon standing for several days and by the application of external cooling it was clear that the isomers could not be separated by crystallisation in an analogous fashion to their 1,4-disubstituted equivalents (**106**, see Section 4.2.2). Several crystallisation methods were subsequently attempted employing various solvents but the *cis*- and *trans*- isomers could not be separated.

4.2.4.3 Synthesis of Polymer 13 from a mixture of *cis*- and *trans*-1,3-bis(bromomethyl)cyclohexane.

The mixture of *cis*- and *trans*-1,3-bis(bromomethyl)cyclohexane (**113**) was next used in the polymer forming step (Scheme 4.15).



113 **Polymer 13**

Scheme 4.15: Synthesis of **Polymer 13** from a mixture of *cis*- and *trans*-1,3-bisbromomethylcyclohexanes (**113**).

A range of conditions were utilised for this polymer forming step in order to obtain more information on the degree of reactivity of this substrate. The results are shown in Table 4.4.

Table 4.4: Products from the different conditions applied for the synthesis of **Polymer 13** from 1,3-bis(bromomethyl)cyclohexanes. [a]

Conditions	Time/ h	Remaining CH_2Br groups. %[b]	Yield/ %
Neat, 170°C,	24	32	41
Neat, 170°C	48	27	37
Ethanol, 95°C,	6	<3	63

[a]A mixture of *cis*- and *trans*-bis(bromomethyl)cyclohexanes (**113**) were reacted with 1.5 mole equivalents of sodium sulfide under the stated conditions. See Scheme 4.15.

[b] The percentage of CH_2Br groups remaining relative to the newly formed CH_2S groups as determined by ^{1}HNMR integrations.

Table 4.4 indicates that the reaction proceeded slowly under the standard Method B conditions but under the refluxing ethanol method the reaction proceeded fairly quickly to go near to completion after 6 hours. The M_n of the polymer obtained from the refluxing ethanol method was determined as 1550 by GPC.

In their ^{13}CNMR spectra, 3-(hydroxymethyl)cyclohexylmethanol (**112**), 1,3-bis(bromomethyl)cyclohexane (**113**) and **Polymer 13** all gave rise to 10 signals. Five signals are expected from the *cis*-isomer, where the two substituents are equatorial (Figure 4.1). However, we would expect to see more than 5 signals for the *trans*-isomer as one of its substituents is equatorial and the other is axial. However, we persistently see a total of 10 signals, 5 signals for this *cis*- isomer and therefore 5 signals also from the *trans*-isomer, unless there are coincidental overlaps. It is likely that 5 signals might be observed from the *trans*-isomer if a time averaged spectrum is 'seen' by ^{13}CNMR. It is conceivable that the ring in the *trans*-1,3-cyclohexane system would flip quickly as the energy in both conformations would be similar as there would be one axial and one equatorial substituent present in each form (Figure 4.1).

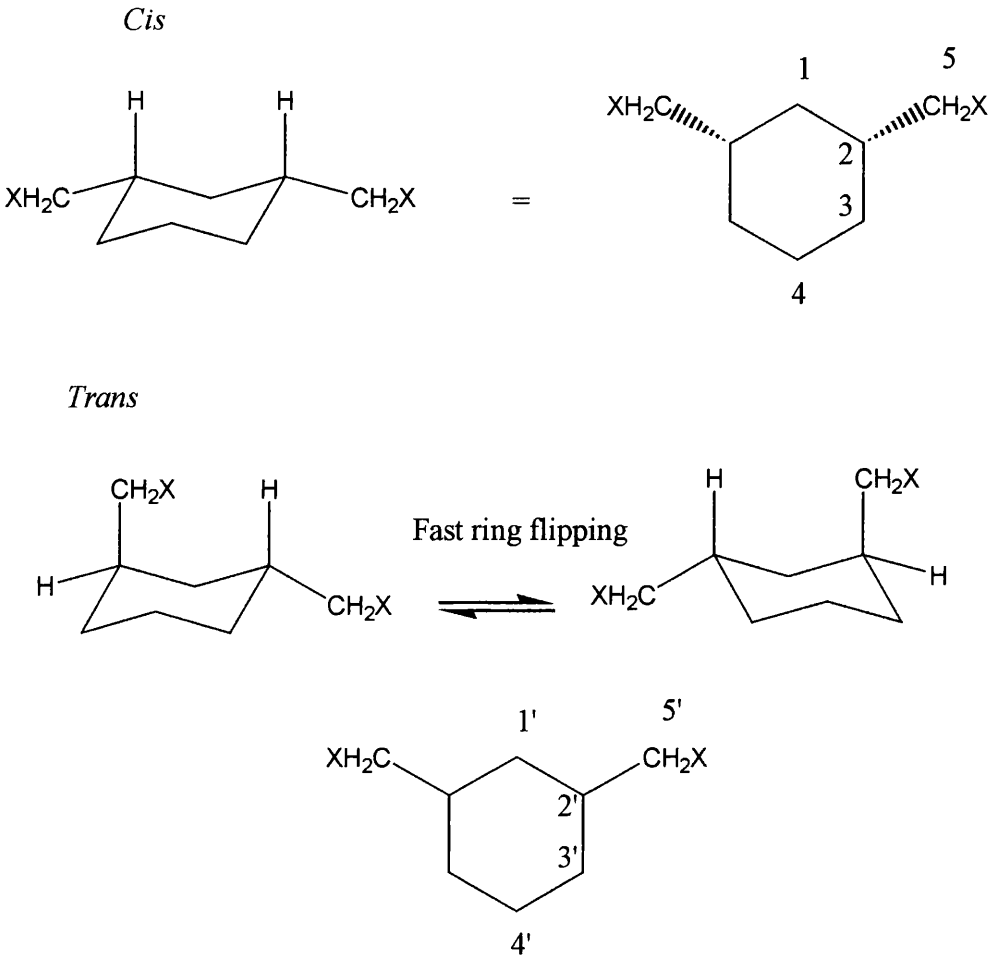
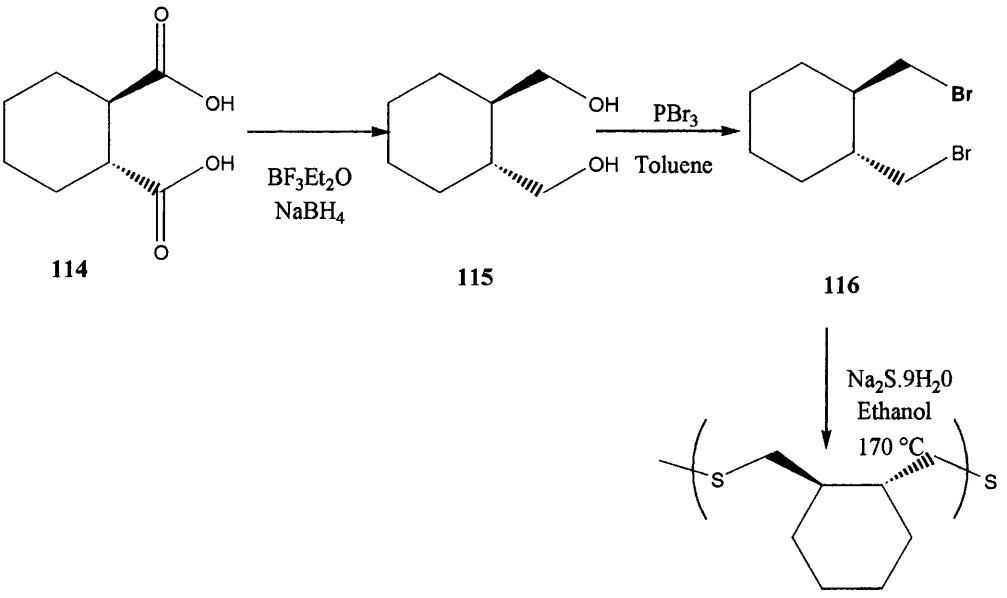


Figure 4.1: A representation of the observable carbons by ^{13}CNMR spectroscopy in *cis*- and *trans*-1,3-disubstituted cyclohexanes.

4.2.5 Attempted synthesis of Polymer 14 from *trans*-1,2-bis(bromomethyl)cyclohexane.

The same procedures described in Section 4.2.4 were applied to the commercially available *trans*-1,2-cyclohexanedicarboxylic acid (**114**) in order to obtain the *trans*-1,2-bis(bromomethyl)cyclohexane (**116**) required for the polymer step (Scheme 4.16).



Scheme 4.16: Proposed synthetic route to **Polymer 14;** reduction of *trans*-cyclohexane-1,2-dicarboxylic acid (**114**) to *trans*-2-(hydroxymethyl)cyclohexylmethanol (**115**) followed by PBr_3 substitution to give *trans*-1,2-bis(bromomethyl)cyclohexane (**116**) required for the Method B polymer forming step.

The reduction step proceeded once again in a quantitative fashion. The reaction was once again conducted on two different scales. The initial reaction was carried out on a small scale to ensure the reaction proceeded sufficiently for this substrate and a second larger scale reaction was carried out to obtain a sufficient amount of the diol (**115**) for the next two synthetic steps. The results are shown in Table 4.5.

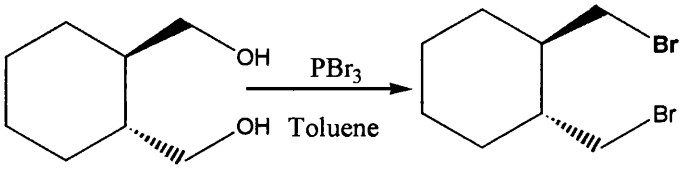
Table 4.5: Product yields from the reduction of *trans*-cyclohexane-1,2-dicarboxylic acid by diborane.

Reaction scale, mmol of cyclohexane-1,2-dicarboxylic acid	Yield of **115**/ mol %[b]	Appearance	Mp/ °C
5.1	97.9	White crystals	62-64
20.5	97.2	White crystals	63-65

[a] *trans*-Cyclohexane-1,2-dicarboxylic acid was refluxed in dry THF in the presence of BF_3Et_2O and $NaBH_4$ for 6 h. See Scheme 4.16.

[b] Isolated yield obtained after reduced pressure distillation and re-crystallisation from hot methanol.

The isolated *trans*-2-(hydroxymethyl)cyclohexylmethanol (**115**) was used in the next step (Scheme 4.17), where it was reacted with PBr_3 under the same conditions used in previous reactions (see Section 4.2.4.2).



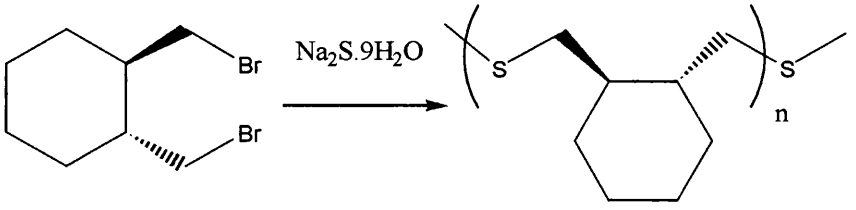
115 **116**

Scheme 4.17: Phosphorus tribromide substitution of *trans*-2-(hydroxymethyl)cyclohexylmethanol (**115**) to give *trans*-1,2-bis(bromomethyl)cyclohexane (**116**).

The reaction proceeded successfully to give a 54 % isolated yield of *trans*-1,2-bis(bromomethyl)cyclohexane (**116**) after reduced pressure distillation.

4.2.5.1 Attempted synthesis of Polymer 14 by the reaction of *trans*-1,2-bis(bromomethyl)cyclohexane with sodium sulfide.

The trans-1,2-bis(bromomethyl)cyclohexane (**116**) was used in the final polymer forming step (Scheme 4.18).



116

Scheme 4.18: Attempted synthesis of **Polymer 14** by the reaction of *trans*-1,2-bis(bromomethyl)cyclohexane (**116**) with sodium sulfide.

Once again the same set of conditions was applied to the dibromide (**116**). The standard Method B conditions were used for 24 hours, then for 48 hours, and thirdly the ethanol reflux was used for 6 hours. In every case the recovery of organic material was low (see Section 4.5.19). The ^{1}HNMR spectrum of each product contained many signals, indicating that a mixture of products was obtained. In each case the spectrum showed signals at around 2.5 ppm which could be due to CH_2S groups. However, in each product the spectrum clearly showed persistent and significant impurities of

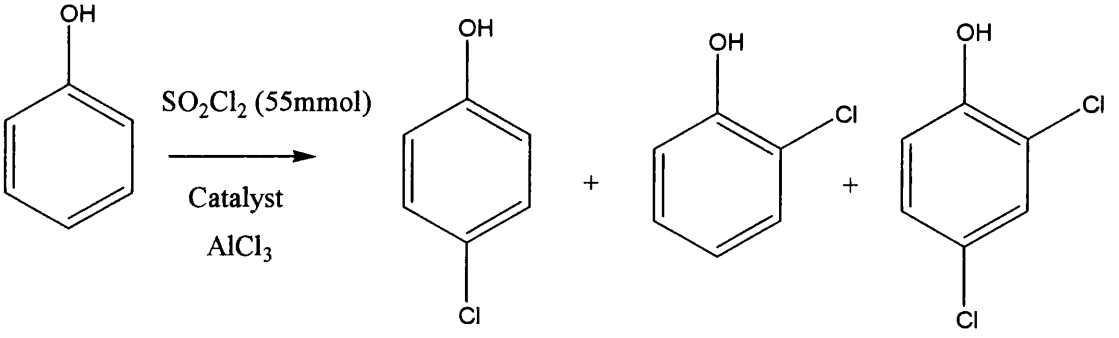
aromatic material and remaining CH_2Br groups. These impure crude products were not tested as catalysts for the chlorination of phenols and no further attempts for the formation of **Polymer 14** were undertaken.

4.3 Chlorination results using novel aromatic and cyclic aliphatic ring containing thiapolymers .

The cyclic aliphatic and aromatic containing thiapolymers synthesised as reported in this chapter were tested as catalysts for the chlorination of phenols and the results are reported in this section.

4.3.1 Chlorination of phenol.

The novel aromatic and cyclic aliphatic ring containing thiapolymers were first tested as catalysts for the chlorination of phenol (Scheme 4.19).



P (50 mmol) **PCP** **OCP** **DCP**

Scheme 4.19: The chlorination of phenol.

The baseline results for the chlorination of phenol in the absence of a sulfide catalyst reported in Section 2.15.2 are recorded again in Table 4.6 for ease of reference.

Table 4.6: Baseline results for the reaction of phenol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	P/ mol %	OCP/ mol %	PCP/ mol %	2,4-DCP/ mol %	*p:o* ratio	Mass balance
-	8.2	21.1	63.7	0.7	3.0	93.7
$AlCl_3$	10.7	17.1	70.1	1.0	4.1	98.9

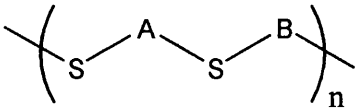
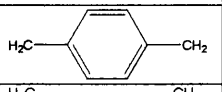
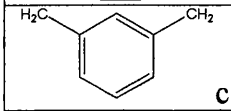
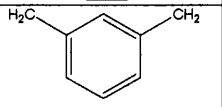
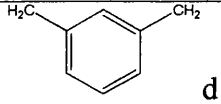
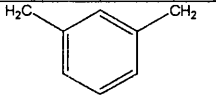
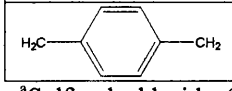
[a] Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (0.375 mmol). For more details see Section 2.15.2.

[b] See Scheme 4.19.

4.3.1.1 Chlorination of phenol using aromatic ring containing thiapolymers.

The aromatic containing thiapolymers synthesised in this chapter were used as catalysts for the chlorination of phenol under the standard reaction conditions reported in Section 2.15.2. The results are shown in Table 4.7.

Table 4.7: Chlorination of phenol with sulfuryl chloride using aromatic containing thiapolymers as catalysts.[a]

Catalyst 							
A	**B**	**P/ mol %** [b]	**OCP/ mol %** [b]	**PCP/ mol %** [b]	**2,4-DCP/ mol %** [b]	***p:o* ratio**	**Mass balance**
		1.6	8.6	86.5	1.3	10.1	98.0
 c		6.4	10.3	83.0	0.0	8.1	99.7
 d		4.8	10.8	82.0	0.0	7.6	97.6
	ethylene	6.5	9.4	81.6	0.8	8.7	98.3
	propylene	1.9	10.8	86.7	0.7	8.0	100.1
	butylenes	9.7	12.5	77.0	1.0	6.2	100.2
	pentylene	5.6	11.7	81.5	1.0	7.0	99.8
	hexylene	9.7	7.1	81.9	0.4	11.5	99.1
	octylene	5.8	8.1	84.7	0.4	10.5	99.0
	decylene	7.8	7.5	83.4	0.4	11.1	99.1

[a]Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.2.

[b] See Scheme 4.19.

[C] Synthesised at 170 °C (see Section 4.1.1).

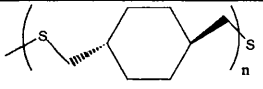
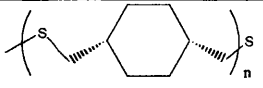
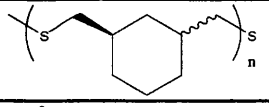
[d] Synthesised by ethanolic reflux (see Section 4.1.1).

It is clear from Table 4.7 that all the polymeric catalysts bring about a favourable enhancement in the *p:o* ratios relative to the 4.1 observed in the baseline result. There is no great disparity in the range of selectivities obtained with these aromatic containing polymers, but the polymers containing the larger spacing units do appear to be marginally more selective. As expected the two *meta* substituted dibenzyl polymers synthesised by Method A and Method B both performed in a very similar manner with selectivity ratios of 8.1 and 7.6 respectively.

4.3.1.2 Chlorination of phenol using cyclic aliphatic ring containing thiapolymers

The cyclic aliphatic ring containing thiapolymers synthesised as reported in this chapter were then tested as catalysts for the chlorination of phenol under the standard reaction conditions reported in Section 2.15.2. The results are shown in Table 4.8.

Table 4.8: Chlorination of phenol using cyclic aliphatic containing thiapolymers[a]

Catalyst	Polymer	P/ mol %[b]	OCP/ mol %[b]	PCP/ mol %[b]	2,4-DCP/ mol %[b]	*p:o* ratio	Mass balance
 *trans-*	**12a**	0.0	8.7	83.8	4.5	9.6	97.0
 *cis-*	**12b**	3.3	6.6	89.4	0.5	13.5	99.8
50:50 *cis-* and *trans-*[c]	**12a/12b (w/w)**	7.6	5.7	86.5	0.7	15.2	100.5
	**13**	1.9	10.2	85.9	1.2	8.4	99.2

[a]Sulfuryl chloride (55 mmol) was reacted with phenol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.2.

[b] See Scheme 4.19.

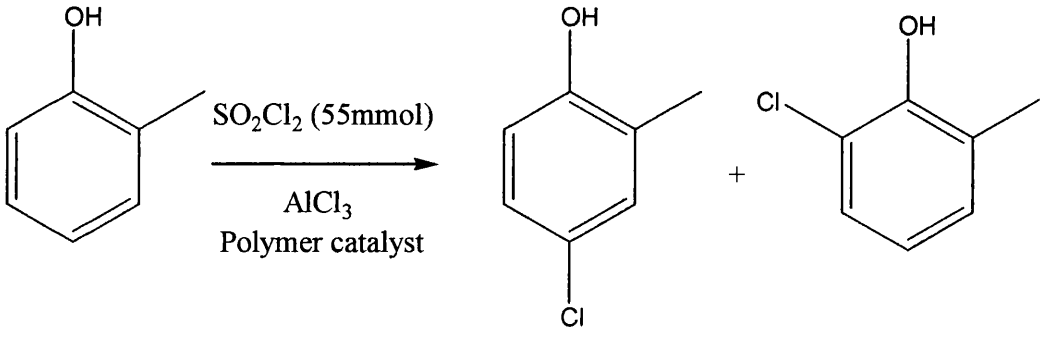
[c] A 50/50 (w/w) mixture of **Polymer 12a** and **Polymer 12b**.

Once again it can be concluded that these polymeric materials clearly catalyse the reaction and enhance the *para* selectivities. The most selective catalyst was the 50-50 (w/w) mixture of the *cis-* and *trans-*1,4-disubstituted cyclohexane thiapolymer,

which surprisingly gave a selectivity of 15.2, which is considerably higher than the average of the selectivities obtained when the individual component polymers where used separately (9.6 and 13.5). This was unexpected and in the first instance suggested a potential anomaly in the result. Alternatively, it may simply be that the interaction of the two different polymers in solution generates a distinct environment which does not behave intermediately of the two components.

4.3.2 Chlorination of *o*-cresol.

The novel aromatic and cyclic aliphatic ring containing thiapolymers were next tested as catalysts for the chlorination of *o*-cresol (Scheme 4.20).



OC (50mmol) **PCOC** **OCOC**

Scheme 4.20: The chlorination of *o*-cresol.

The baseline results for the chlorination of *o*-cresol in the absence of a sulfide catalyst reported in Section 2.15.4 are recorded again in Table 4.9 for ease of reference.

Table 4.9: Baseline results for the chlorination of *o*-cresol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Catalyst	$AlCl_3$ (g)	OC mol%[b]	OCOC mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
—	—	2.0	15.4	78.2	5.1	95.6
—	0.05	9.6	11.9	75.1	6.3	96.6

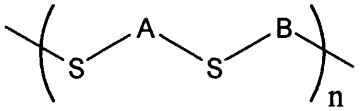
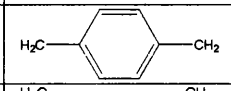
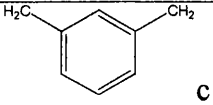
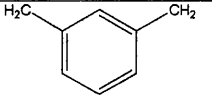
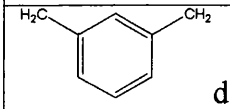
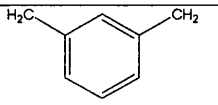
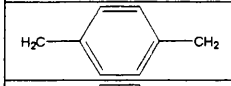
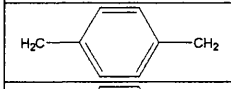
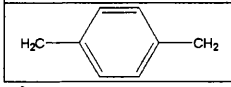
[a] Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (0.375 mmol). For more details see Section 2.15.4.

[b] See Scheme 4.20.

4.3.2.1 Chlorination of *o*-cresol using aromatic ring containing thiapolymers.

The aromatic ring containing thiapolymers synthesised in this chapter were tested as catalysts for the chlorination of *o*-cresol under the standard reaction conditions reported in Section 2.15.4. The results are shown in Table 4.10.

Table 4.10: Chlorination of *o*-cresol with sulfuryl chloride using aromatic ring containing thiapolymers as catalysts. [a]

Catalyst  **A**	**B**	**OC mol%** [b]	**OCOC mol%** [b]	**PCOC mol%** [b]	***p:o* ratio**	**Mass balance**
		2.7	3.1	91.6	29.5	97.4
 c		10.8	3.3	85.0	25.8	99.1
 d		2.6	6.7	90.1	13.4	99.4
	ethylene	1.8	11.2	84.9	7.6	97.9
	propylene	3.2	3.2	91.8	28.7	98.2
	butylenes	3.5	13.1	77.3	5.9	93.9
	pentylene	8.1	8.3	83.5	10.1	99.9
	hexylene	5.6	8.5	82.8	9.7	96.9
	octylene	4.0	10.4	82.8	8.0	97.2
	decylene	6.2	4.8	88.4	18.4	99.4

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.4.

[b]See Scheme 4.20.

[c] Synthesised at 170 °C (see Section 4.1.1).

[d] Synthesised by ethanolic reflux (see Section 4.1.1).

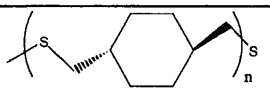
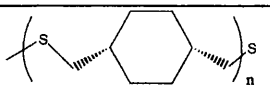
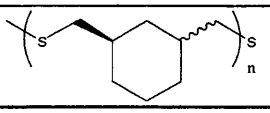
Table 4.10 clearly indicates a large disparity in the selectivities obtainable with these aromatic containing polymers. Most notably, there appears to be a significant difference in the reactivity of the two seemingly identical *meta* substituted aromatic thiapolymers and it is likely that one of the results is an anomaly. It is more likely that the least selective result is actually an anomaly as there are many potential mechanisms that could lead to the reduction in the *para* selectivity such as 1) polymeric material becoming deposited on the walls of the vessel and therefore not being available in solution to act as a selective catalyst; 2) poor control of the addition of sulfuryl chloride (see Section 2.15.3) resulting in the exothermic heating of the reaction which results in lower *para* selectivity;[6] 3) abnormal levels of moisture resulting in the breakdown of the Lewis acid; 4) the sulfuryl chloride may have deteriorated resulting in the generation of the less selective chlorinating agent molecular chlorine. Neither experiment has been repeated due to restraints on time.

The *para* dibenzyl polymer performed well and gave a high selectivity ratio of 29.5. Out of the semi-aromatic thiaalkanes it is clear that the polymer containing a propylene spacing unit is by far the most selective. Previous results within the research group[2] have shown that the propylene spacing group is inexplicably more effective than similar spacing groups, with polymers possessing it being more selective than analogous polymers without it for the chlorination of *o*-cresol. It is speculated that there might be an interaction between one of the sulfur atoms with the hydroxyl group which results with the other sulfur (chlorosulfonium) being in the proximity of the *para* position. The propylene containing polymer was subjected to further investigation (see Section 4.3.2.3)

4.3.2.2 Chlorination of *o*-cresol using cyclic aliphatic ring containing thiapolymers.

The cyclic aliphatic ring containing thiapolymers synthesised as reported in this chapter were then tested as catalysts for the chlorination of *o*-cresol under the standard reaction conditions reported in Section 2.15.4. The results are shown in Table 4.11.

Table 4.11: Chlorination of *o*-cresol using cyclic aliphatic containing thiapolymers[a]

Catalyst	Polymer	OC mol%[b]	OCOC Mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
 *trans-*	**12a**	3.7	3.8	89.7	23.6	97.2
 *cis-*	**12b**	4.4	2.8	87.9	31.4	95.1
50:50 *cis-* and *trans-*[c]	**12a/12b (w/w)**	5.1	4.6	87.0	18.9	96.7
	**13**	2.8	2.6	93.3	35.9	98.7

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and a polymeric sulfide (0.284 mmol). For more details see Section 2.15.4.

[b]See Scheme 4.20.

[c] A 50/50 (w/w) mixture of **Polymer 12a** and **Polymer 12b**.

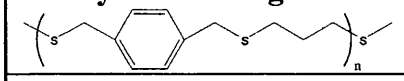
The *cis-* and *trans*-1,4-disubstituted cyclohexane thiapolymers both performed well as selective catalysts with selectivity ratios of 23.6 and 31.4 respectively. Once again the 50/50 mixture of the *cis-* and t*rans-* did not behave in an intermediate manner to the individual components and gave a selectivity of 18.9, which is considerably lower than the average of the two component polymers.

The 1,3-disubstituted cyclohexane thiapolymer gave a very high selectivity of 35.9 with 93.3 % of the desired *para* product accounted for. More reactions were conducted using this polymer as a catalyst for the chlorination of *o*-cresol and the results are reported in Section 4.3.4.2.

4.3.2.3 Chlorination of *o*-cresol using various amounts of poly(sulfanediylmethylene-1,4-phenylenemethyenesulfanediylpropane-1,3-diyl).

The selective polymer synthesised from the Method A reaction of 1,3-propanedithiolate and α,α'-dibromo-*p*-xylene (see Section 4.1.4), as reported in Table 4.10 was used as a catalysts in a series of reactions employing various amounts of the catalyst. The results are shown in Table 4.12.

Table 4.12: Chlorination of *o*-cresol using varying amounts of poly(sulfanediylmethylene-1,4-phenylenemethylenepropane-1,3-diyl).[a]

Catalyst mmol/mg 	OC mol%[b]	OCOC mol%[b]	PCOC mol%[b]	*p:o* ratio	Mass balance
0.682/120	4.6	2.8	89.9	32.1	97.3
0.568/100	3.9	2.9	91.6	31.6	98.4
0.284/ 60[c]	3.2	3.2	91.8	28.7	98.2
0.190/40	6.2	3.0	90.8	30.3	100.0
0.071/ 15	6.7	3.2	85.5	26.7	95.4
0.036/ 7.5	12.0	6.7	81.7	12.2	100.4

[a] Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) and this aromatic sulfide catalyst. For more details see Section 2.15.4.

[b]See Scheme 4.20.

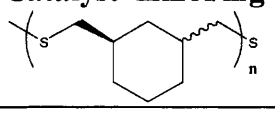
[c]As first shown in Table 4.10.

Table 4.12 shows that doubling the amount of the catalyst employed from 60 mg to 120 mg only resulted in a marginal increase in the *para* selectivity from 28.7 to 32.1. By reducing the amount to 40 mg a marginally higher value of 30.3 was observed, which then dropped a small amount to 26.7 when 15 mg was used. The high selectivity can no longer be retained when only 7 mg was employed; instead a selectivity value of 12.2 was observed. The selectivity of 26.7 in the presence of only 15 mg of catalysts appeared to be the most promising result. However, this catalyst was not investigated any further as attention was turned to the use of **Polymer 13** (see Table 4.11), which was deemed to be even more selective after the initial experiments under standard conditions.

4.3.2.4 Chlorination of *o*-cresol using various amounts of Polymer 13.

The selective 1,3-disubstituted cyclohexane thiapolymer (**Polymer 13**), as reported in Table 4.10, was used as a catalyst in a series of reactions employing various amounts of the catalyst. The results are shown in Table 4.13

Table 4.13: Chlorination of *o*-cresol using various amounts of **Polymer 13**. [a]

Catalyst mmol/mg 	**OC mol%**[b]	**OCOC mol%**[b]	**PCOC Mol%**[b]	***p:o* ratio**	**Mass balance**
0.710/200	0.7	1.7	95.4	56.1	97.8
0.568/160	9.2	1.8	88.5	49.2	99.5
0.426/120	12.2	2.0	85.2	42.6	99.4
0.355/100	26.9	1.7	70.6	41.5	99.2
0.284/80[c]	2.8	2.6	93.3	35.9	98.7
0.142/40	4.0	2.1	91.9	43.8	98.0
0.071/20	7.3	2.4	90.0	37.5	99.7
0.036/10	5.6	2.3	90.6	39.4	98.5
0.013/5	4.4	3.6	91.9	25.5	99.9

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of $AlCl_3$ (0.375 mmol) with various amounts of **Polymer 13** as a catalyst. For more details see Section 2.15.4.

[b]See Scheme 4.20.

[c]As first shown in Table 4.11.

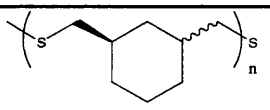
Table 4.13 clearly shows that by increasing the amount of the catalyst used then the *para* selectivity can be increased. By using 200 mg (0.71 mmol) of the polymer instead of the original 80 mg an increase in the selectivity value from 35.9 to 56.1 and an increase in the yield of the *para* product from 93.3 to 95.4 % were observed.

Table 4.13 also indicates that this catalyst also retained its selectivity exceptionally well when decreasing amounts were employed. In fact, by halving the amount used to 40 mg an increase in the selectivity value was observed from 35.9 to 44.0. Even when only 10 mg of polymer was used a selectivity value of 39.4 was obtained which is marginally higher than the original value when 80 mg of catalyst was employed. When only 5 mg of the catalyst was used a selectivity value of 25.5 was obtained, which still represents an excellent increase in selectivity relative to the baseline result. However, on balance the use of 10 mg was deemed to give rise to the most significant result and was therefore the amount used in further investigations, where the main objective was maintaining the high selectivity in the presence of decreasing amounts of the Lewis acid co-catalyst.

4.3.2.5 Chlorination of *o*-cresol using 10 mg of Polymer 13 as a catalyst with various amounts of $AlCl_3$ co-catalyst.

The use of 10 mg of **Polymer 13** as a catalyst for the chlorination of *o*-cresol was further investigated in the presence of various amounts of the Lewis acid co-catalyst ($AlCl_3$) and the results are shown in Table 4.14.

Table 4.14: Chlorination of *o*-cresol using with **Polymer 13** with varying amounts of $AlCl_3$.[a]

 Amount of $AlCl_3$ / mg	**OC mol%**	**OCOC mol%** [b]	**PCOC mol%**	***p:o* ratio**	**Mass balance**
200	13.5	3.0	80.7	26.9	97.3
100	6.6	2.4	90.9	37.9	99.9
50[c]	5.6	2.3	90.6	39.4	98.5
40	7.3	2.7	88.4	32.7	98.4
30	3.5	2.8	93.1	33.3	99.4
20	14.5	2.3	81.5	35.4	98.3
10	5.2	3.5	90.8	25.9	99.5
5	11.3	3.6	84.7	23.5	99.6
3	4.7	4.9	90.0	18.4	99.6

[a]Sulfuryl chloride (55 mmol) was reacted with *o*-cresol (50 mmol) in the presence of **Polymer 13** (10mg, 0.036 mmol) with various amounts of $AlCl_3$ co-catalyst. For more details see Section 2.15.4. See Scheme 4.20.

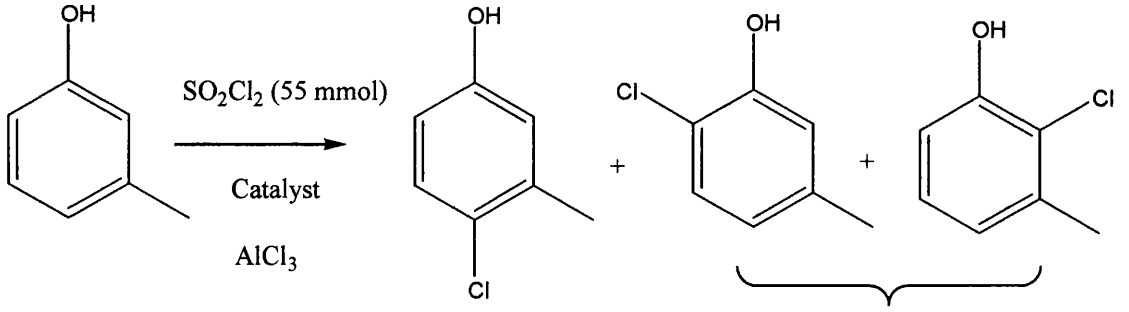
[c]As first seen in Table 4.13.

As the amount of the Lewis acid was increased from 50 mg to 100 mg then there appeared to be very little change in the reaction products obtained. A further increase to 200 mg actually resulted in a drop in the obtained selectivity from 39.4 to 26.7.

Table 4.14 shows that decreasing the amount of Lewis acid employed resulted in the expected decrease in the *para* selectivity. However, as hoped, the selectivity value did not drop sharply and when only 20 mg of the Lewis acid was used a very high selectivity of 35.4 was still obtainable. Below that point the selectivity value did begin do drop more significantly but in the presence of only 3 mg of the Lewis acid a selectivity of 18.4 and a yield of 90.0 % of the desired *para* chlorinated product was obtained

4.3.3 Chlorination of *m*-cresol.

The novel aromatic and cyclic aliphatic ring containing thiapolymers were next tested as catalysts for the chlorination of *m*-cresol (Scheme 4.21).



MC (50 mmol) **PCMC** **OCMC**

Scheme 4.21: The chlorination of *m*-cresol.

The baseline results for the chlorination of *m*-cresol in the absence of a sulfide catalyst reported in Section 2.15.6 are recorded again in Table 4.15 for ease of reference.

Table 4.15: Baseline results for the chlorination of *m*-cresol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	MC/ Mol %[b]	OCMC/ mol %[b,c]	PCMC/ mol %[b]	*p:o* ratio	Mass balance
-	8.7	12.5	78.3	6.3	99.5
$AlCl_3$	14.2	10.0	75.8	7.6	100.0

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $AlCl_3$ (1.875 mmol). For more details see Section 2.15.6.

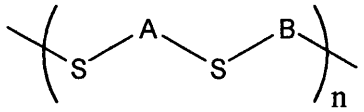
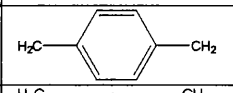
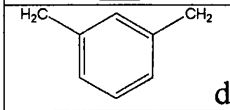
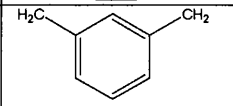
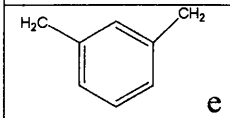
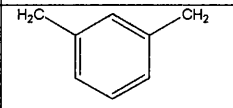
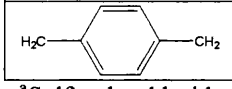
[b] See Scheme 4.21.

[c] Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

4.3.3.1 Chlorination of *m*-cresol using aromatic ring containing thiapolymers.

The aromatic containing thiapolymers synthesised in this chapter were tested as catalysts for the chlorination of *m*-cresol under the standard reaction conditions reported in Section 2.15.6. The results are shown in Table 4.16.

Table 4.16: Chlorination of *m*-cresol using aromatic containing thiapolymers.[a]

Catalyst 		**MC/ mol %**[b]	**OCMC/ mol %**[b,c]	**PCMC/ mol %**[b]	***p:o* ratio**	**Mass balance**
A	**B**					
		17.9	6.8	75.1	11.0	99.8
 d		2.2	7.2	87.9	12.2	97.3
 e		7.7	7.6	84.3	11.1	99.6
	ethylene	12.0	6.8	79.4	11.7	98.2
	propylene	7.1	7.8	81.5	10.4	96.4
	butylenes	12.6	6.6	80.3	12.2	99.5
	pentylene	1.3	6.5	90.0	13.8	97.8
	hexylene	23.1	5.1	71.3	14.0	99.5
	octylene	2.0	6.0	91.2	15.2	99.2
	decylene	5.0	5.7	88.8	15.6	99.5

[a]Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the presence of $AlCl_3$ (1.875 mmol) and a polymeric sulfide catalyst (0.403 mmol). For more details see Section 2.15.6.

[b]See Scheme 4.21.

[c]Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

[d]Synthesised at 170 °C (see Section 4.1.1).

[e]Synthesised by ethanolic reflux (see Section 4.1.1).

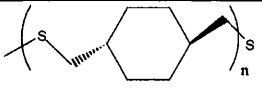
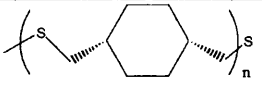
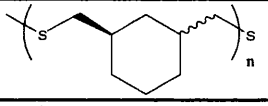
In the presence of these aromatic containing polymers moderate increases (approximately 1.5-2 times higher than the baseline results) are obtained. Once again the polymers containing the larger aliphatic spacing units appear to be marginally more selective. However, no results show the desired significant increase in the *para*

selectivity and therefore no further experiments were carried out using these polymers.

4.3.3.2 Chlorination of *m*-cresol using cyclic aliphatic ring containing thiapolymers.

The cyclic aliphatic ring containing thiapolymers synthesised in this chapter were tested as catalysts for the chlorination of *m*-cresol under the standard reaction conditions reported in Section 2.15.6. The results are shown in Table 4.17.

Table 4.17: Chlorination of *m*-cresol with sulfuryl chloride using cyclic aliphatic containing thiapolymers as catalysts. [a]

Catalyst	Polymer	MC/ mol %[b]	OCMC/ mol %[b,c]	PCMC/ mol %[b]	*p:o* ratio	Mass balance
 *trans-*	**12a**	6.9	4.5	86.6	19.2	98.0
 *cis-*	**12b**	7.3	4.7	86.8	18.5	98.8
50:50 *cis-* and *trans-*[d]	**12a/12b (w/w)**	15.9	3.9	78.3	20.1	98.1
	**13**	1.5	3.0	93.6	31.2	98.1

[a]Sulfuryl chloride (55 mmol) was reacted with *m*-cresol (50 mmol) in the presence of $AlCl_3$ (1.875 mmol) and a polymeric sulfide catalyst (0.403 mmol). For more details see Section 2.15.6.

[b]See Scheme 4.21.

[c]Mixture of 2-chloro-3-methylphenol and 2-chloro-5-methylphenol.

[d] A 50/50 (w/w) mixture of **Polymer 12a** and **Polymer 12b**.

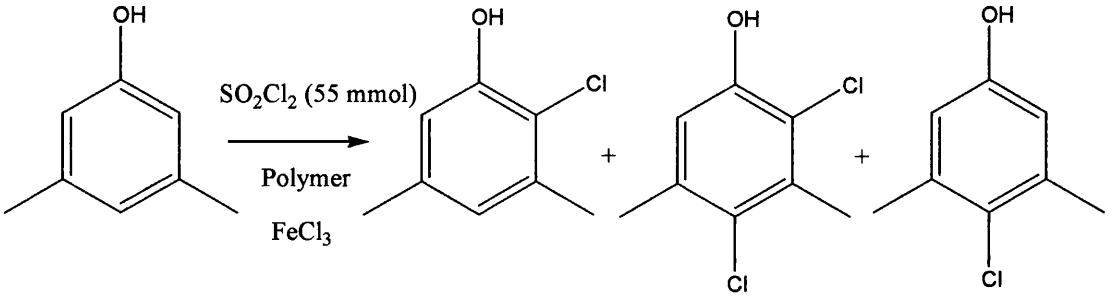
The *trans-* and *cis-*1,4-disubstituted cyclohexane thiapolymers both performed reasonably well as selective catalysts with selectivity ratios of 19.2 and 18.5 obtained respectively. This time the behaviour of the 50/50 mixture was similar to its corresponding individual components with a selectivity value of 20.1.

The 1,3-disubstituted cyclohexane thiapolymer that proved to be highly selective for *o*-cresol also appears to be a very promising catalyst for the chlorination of *m*-cresol with a ratio of 31.2 and a yield of 93.6 % of the desired *para* product

obtainable. However, due to time constraints no further investigation of the chlorination of *m*-cresol with this polymer has been conduct.

4.3.4 Chlorination of *m*-xylenol.

The novel aromatic and cyclic aliphatic ring containing thiapolymers were next tested as catalysts for the chlorination of *m*-xylenol (Scheme 4.22).



MX (50 mmol) **OCMX** **DCMX** **PCMX**

Scheme 4.22: The chlorination of *m*-xylenol.

The baseline results for the chlorination of *m*-xylenol in the absence of a sulfide catalyst reported in Section 2.15.8 are recorded again in Table 4.18 for ease of reference.

Table 4.18: Baseline results for the reaction of *m*-xylenol with sulfuryl chloride in the absence of a sulfide catalyst.[a]

Lewis acid	MX/ mol %	OCMX/ mol %	PCMX/ mol %	DCMX/ mol %	*p:o* ratio	Mass balance
-	13.4	9.8	68.6	0.0	7.0	91.8
$FeCl_3$	15.4	10.3	71.1	0.0	6.9	96.8

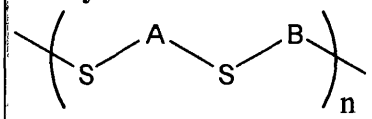
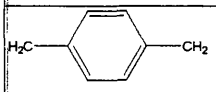
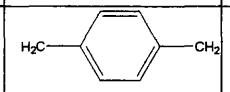
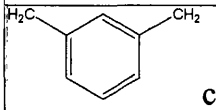
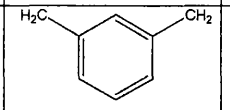
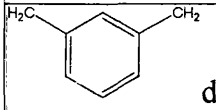
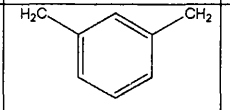
[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the absence of a sulfide catalyst with and without the presence of $FeCl_3$ (0.154 mmol). For more details see Section 2.15.8

[b] See Scheme 4.22.

4.3.4.1 Chlorination of *m*-xylenol using aromatic ring containing thiapolymers.

The aromatic containing thiapolymers synthesised as reported in this chapter were tested as catalysts for the chlorination of *m*-xylenol under the standard reaction conditions reported in Section 2.15.8. The results are shown in Table 4.19.

Table 4.19: Chlorination of *m*-xylenol with sulfuryl chloride using aromatic ring containing thiapolymers as catalysts. [a]

Catalyst  **A**	**B**	**MX/ mol %** [b]	**OCMX/ mol %** [b]	**PCMX/ mol %** [b]	**DCMX/ mol %** [b]	***p:o* ratio**	**Mass balance**
		5.1	8.0	86.1	0.0	10.8	99.2
 c		0.0	8.9	85.0	4.6	9.6	98.5
 d		6.2	7.9	81.8	3.0	10.4	98.9
	ethylene	16.2	7.3	75.7	0.0	10.4	99.2
	propylene	10.5	9.7	77.2	0.0	8.0	97.4
	butylenes	9.9	8.2	80.1	0.0	9.8	98.2
	pentylene	6.1	6.9	83.9	0.9	12.2	97.8
	hexylene	5.7	5.3	85.2	3.7	16.1	99.9
	octylene	8.4	8.1	82.1	0.5	10.1	99.1
	decylene	13.8	6.0	78.7	0.0	13.1	98.5

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) and a polymeric sulfide catalyst (0.052 mmol). For more details see Section 2.15.8

[b] See Scheme 4.22.

[c] Synthesised at 170 °C (see Section 4.1.1).

[d] Synthesised by ethanolic reflux (see Section 4.1.1).

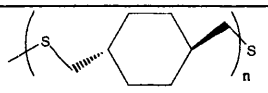
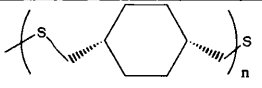
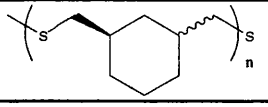
In a similar manner to that observed for *m*-cresol and phenol all these aromatic containing polymers are shown to give only moderate increases in the *para* selectivity values. When the hexylene containing polymer was used a relatively high ratio of 16.1 was obtained. However, in this reaction a significant amount (3.7 %) of the dichlorinated product had formed. Obviously the **DCMX** was formed from either

PCMX or **OCMX**. Considering that *para* chlorination is far more favourable than *ortho* chlorination, then it can be assumed that a more than proportionate amount of **DCMX** was formed from **OCMX**, and therefore giving rise to a 'false' increase in the *para:ortho* selectivity value, which is not a true representation of the selectivity obtained under these conditions.

4.3.4.2 Chlorination of *m*-xylenol using cyclic aliphatic ring containing thiapolymers.

The cyclic aliphatic ring containing thiapolymers synthesised in this chapter were then tested as catalysts for the chlorination of *m*-xylenol under the standard reaction conditions reported in Section 2.15.8. The results are shown in Table 4.20.

Table 4.20 : Chlorination of *m*-cresol with sulfuryl chloride using cyclic aliphatic ring containing thiapolymers as catalysts.[a]

Catalyst	Polymer	MX/ mol %[b]	OCMX/ mol %[b]	PCMX/ mol %[b]	DCMX/ mol %[b]	*p:o* ratio	Mass balance
 *trans-*	**12a**	4.1	3.0	88.3	4.5	29.4	99.9
 *cis-*	**12b**	10.2	3.7	87.1	0.0	23.5	101.0
50:50 *cis-* and *trans-*[c]	**12a/12b (w/w)**	6.4	4.6	83.4	0.0	18.1	94.4
	**13**	0.0	4.6	93.8	0.8	20.4	99.2

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) and a polymeric sulfide catalyst (0.052 mmol). For more details see Section 2.15.8.

[b] See Scheme 4.22.

[c] A 50/50 (w/w) mixture of **Polymer 12a** and **Polymer 12b**.

In the first instance the trans-1,4-disubstituted cyclohexane thiapolymer appeared to be the most selective catalyst for the chlorination of *m*-xylenol with a *p:o* ratio of 29.4 observed. However, in that reaction there was also 4.5 % of **DCMX** formed. The *cis-* isomer also gave a good selectivity of 23.5. The 50/50 mixture for the third time out of four gave rise to a result significantly different to a value

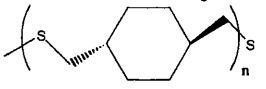
intermediate of its two components. It can be speculated that the environment generated by the mixing of these different polymers is distinct and the resulting selectivity obtained is seemingly independent of that obtained with individual components alone. This is an interesting speculation, and if it is true suggests that the selectivity can be altered by the mixing of different polymers. However, this speculation has not been addressed herein.

The 1,3-disubstituted cyclohexane thiapolymer that proved to be very selective for *ortho* and *meta* cresol also gave rise to a good selectivity value for *m*-xylenol of 20.4 and a yield of 93.8 % of the desired **PCMX**. However, the observed selectivity value is highest when the *trans*-1,4-disubstituted cyclohexane thiapolymer (**Polymer 12a**) was used. This polymer was also more readily available (easier to synthesise) and therefore it was this polymer that was chosen for further investigation (see Section 4.3.4.3).

4.3.4.3 Chlorination of *m*-xylenol with various amounts of Polymer 12a as a catalyst.

The chlorination of *m*-xylenol was then carried out using various amounts of the selective **Polymer 12a** as a catalyst (Table 4.21).

Table 4.21: Chlorination of *m*-xylenol with sulfuryl chloride using various amounts of **Polymer 12a** as a catalyst. [a]

Amount of Polymer  **mmol (mg)**	**MX/ mol %**	**OCMX/ mol %**	**PCMX/ mol %**	**DCMX/ mol %**	***p:o* ratio**	**Mass balance**
0.208(57)	9.5	3.2	87.0	0.0	27.2	99.7
0.104 (29)	4.5	3.0	90.1	0.0	30.0	97.6
0.052 (14)[c]	4.1	3.0	88.3	4.5	29.4	99.9
0.026 (7)	8.3	2.8	89.6	0.0	32.0	100.7
0.013(3.5)	5.4	7.3	84.4	0.0	11.6	97.1

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of $FeCl_3$ (0.154 mmol) with various amounts of **Polymer 12a**. For more details see Section 2.15.8.

[b] See Scheme 4.22.

[c] As first shown in Table 4.20.

When the amount of the polymer used was increased from 14 mg to 29 mg and then to 57 mg the selectivity values changed only slightly to 30.0 and 27.2

respectively. However, it was observed that no **DCMX** was formed in these reactions and therefore the selectivity values obtained are a true representation of the chlorination process, which is almost certainly higher than the selectivity that would have been obtained in the original experiment assuming no **DCMX** had formed. When the amount of the catalyst was halved to 7 mg the selectivity value increased to 32.0 and once again no **DCMX** was obtained making this reaction significantly better than the original in terms of *para* selectivity and in terms of monochlorination. When the amount of the catalyst was halved again the selectivity dropped significantly to 11.6. Further investigation was conducted using 7 mg of the catalyst in the presence of various amounts of the Lewis acid.

4.3.4.4 Chlorination of *m*-xylenol with sulfuryl chloride using Polymer 12a (7 mg) as catalyst in the presence of various amounts of $FeCl_3$.

The chlorination of *m*-xylenol using 7 mg of **Polymer 12a** was repeated using various amounts of the $FeCl_3$ co-catalyst and the results are shown in Table 4.22.

Table 4.22: Chlorination of *m*-xylenol using **Polymer 12a** (7mg) with various amounts of $FeCl_3$

Lewis acid / mg	**MX/ mol %**	**OCMX/ mol %**	**PCMX/ mol %**	**DCMX/ mol %**	***p:o* ratio**	**Mass balance**
25[c]	8.3	2.8	89.6	0.0	32.0	100.7
20	2.3	4.3	92.1	0.8	21.4	99.5
15	3.3	4.2	90.0	0.5	21.4	98.0
10	0.0	5.1	91.8	2.5	18.0	99.4
7.5	0.5	4.3	92.8	0.0	21.6	97.6
5	4.0	5.1	90.7	0.0	17.8	99.8
3	4.3	6.2	88.8	0.0	14.3	99.3

[a] Sulfuryl chloride (55 mmol) was reacted with *m*-xylenol (50 mmol) in the presence of 7 mg of **Polymer 12a** (0.026) mmol) with various amounts $FeCl_3$.

[b] See Scheme 4.22.

[c] As first shown in Table 4.21.

As expected, when the amount of the Lewis acid used was reduced then the observed *para* selectivity also dropped. When the amount used was reduced from 25 to 20 mg the selectivity value fell significantly from 32.0 to 21.4. However, beyond

this point the selectivity was retained fairly well and did not deviate far from a value of 20 until when only 3 mg of Lewis acid was employed and even then a respectable selectivity value of 14.3 was observed.

4.4 Conclusion for chapter 4

Numerous novel aromatic ring and aliphatic ring containing thiapolymers were successfully synthesised and tested as catalysts for the chlorination of phenol, *o*-cresol, *m*-cresol and *m*-xylenol.

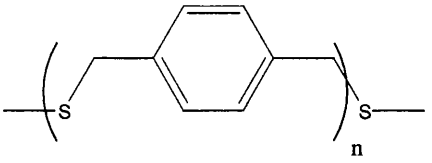
The cyclic aliphatic containing thiapolymers proved to be effective selective catalysts for *o*-cresol, *m*-cresol and *m*-xylenol. The most selective cyclic aliphatic ring containing thiapolymer was shown to be poly(sulfanediylmethylenecyclohexane-1,3-diylmethylene) (**Polymer 13**) which above all showed excellent selectivity for the chlorination of *o*-cresol with high *p:o* selectivities of around 35 obtainable using only 10 mg of catalyst per 50 mmol of substrate in the presence of only 20-50 mg of Lewis acid co-catalyst per 50 mmol of substrate.

See Section 4.6 for final conclusion.

4.5 Experimental

4.5.1 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylene) (Polymer 9).

The standard Method B (see Section 2.18.25) conditions were applied and the following amounts were used: sodium sulfide nonahydrate (6.825 g, 28.4 mmol), α,α'-dibromo-*p*-xylene (5.00 g, 18.9 mmol). After filtration and drying a white powder product was obtained (2.49 g, 97 %). The product was insoluble in dichloromethane, chloroform, DMSO, and trifluoroacetic acid.

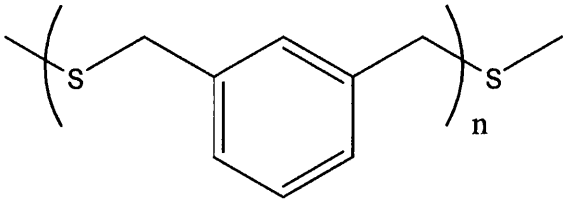


FTIR (neat) *v* 3023, 2909 (C-H *str*) 1907-2335 multiple bands (aromatic C-H), 849 (C-H wag), 699 (C-S str).

4.5.2 Synthesis of poly(sulfanediylmethylene-1,3-phenylenemethylene). (Polymer 10).

Standard Method B conditions were applied and the following amounts were used: sodium sulfide nonahydrate (6.825 g, 28.4 mmol), α,α'-dibromo-*m*-xylene (5.00 g, 18.9 mmol). After filtration and drying a plastic-like white solid was obtained. The white material was stirred vigorously in dichloromethane for several days to eventually yield a whiter powder-like material (2.26 g, 88 %). The product was insoluble in dichloromethane, chloroform, DMSO, and trifluoroacetic acid.

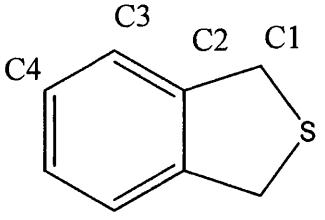
The refluxing ethanol method was also used. Sodium sulfide nonahydrate (6.825 g, 28.4 mmol), α,α'-dibromo-*m*-xylene (5.00 g, 18.9 mmol) and ethanol (25 mL) were added to a 50 mL round bottomed flask fitted with a reflux condenser. The flask was heated to 100 °C using a heater and an oil bath and the mixture was stirred magnetically for 2 hours. The reflux condenser was removed and the ethanol was allowed to evaporate. The mixture was then allowed to cool and was quenched with water (30 mL). The mixture was allowed to stir for 1 hour. The yellow/white precipitate was collected by suction filtration and was then washed thoroughly with water (3 x 50 mL), hexane (3 x 50 mL), and methanol (3 x 50 mL). The powder was dried at 60°C at 2 mmHg of pressure for 4 hours. The white powder product was (1.19 g, 92 %) was insoluble in dichloromethane, chloroform, DMSO, and trifluoroacetic acid.



FTIR (neat)ν 3018, 2915, 2854 (C-H *str*), 797 (C-H wag *meta*) 705, 693 (probably C-H wag *meta*, and C-S str).

4.5.3 Attempted synthesis of poly(sulfanediylmethylene-1,2-phenylenemethylene) and the resulting synthesis of 1,3-dihydrobenzo[c]thiophene

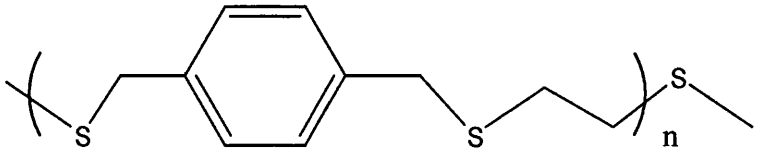
Sodium sulfide nonahydrate (3.41 g, 14.0 mmol) and α,α'-dibromo-*o*-xylene (2.5 g, 9.5 mmol) were added to a 50 mL round bottomed flask fitted with a reflux condenser. The flask was heated to 170 °C using a heater and a silicon oil bath and the mixture was allowed to stir for 4 hours, during which time the mixture turned black. The reaction was allowed to cool and was then quenched with water (30 mL). No precipitate was present. The aqueous phase was extracted with dichloromethane (3 x 30 mL). The phases were separated and the organic phase was dried over $MgSO_4$. The drying agent was filtered off and the organic solvent was removed by rotary evaporation to give a crude black oil (1.12 g). TLC analysis indicated 1 main component with 2 or 3 faint spots representing any other minor components (not starting material). At this stage it was clear that a reaction had occurred but it was unlikely that the desired polymer had formed (as it would have been present as an insoluble precipitate after the quenching stage). It was speculated that an internal substitution step may have occurred to give a dihydrobenzothiophene.The crude product was subjected to reduced pressure kuglerohr distillation (6 mmHg). One component (0.88 g, 68 %) at 90°C was isolated. Lit.[7] 45-57 °C at 1mmHg.
The clear oil turned to a black oil/solid mixture after 48 hours.



^{1}H-NMR ($CDCl_3$) δ 4.45 (4H, s, ArCH_2S), 7.35 (4H, m, ArH).^{13}C-NMR ($CDCl_3$), δ 38.5 (C1), 125.1 (C4), 127.1 (C3), 140.8 (C2). FTIR (neat) *v* 730 (probably C-S str). No C-Br band. MS EI$^+$ m/z 135, ([M-H]$^+$, 100 %) 104 ([M-S]$^+$, 50 %), 73 (60 %), 70 (50 %).

4.5.4 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylenesulfandiylethylene).

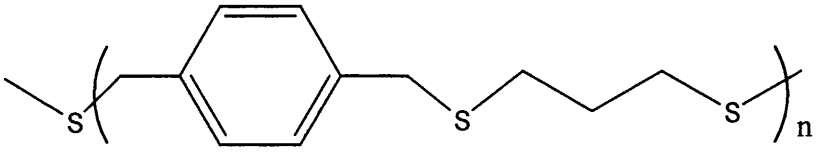
Standard Method A conditions were applied and the following amounts were used: 1,2-ethanedithiol (1.25 mL, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), α,α'-dibromo-*p*-xylene (3.56 g ,13.5 mmol) in dry THF (10 mL) and 1-bromobutane (0.41 g, 3.0 mmol) . After filtration washing and drying a white powder (1.83 g, 62 %) was obtained.



FTIR (neat) *v* 852 (C-H wag *para*), 688 (probably C-S str), no C-Br str.

4.5.5 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylenesulfanediylpropane-1,3-diyl)

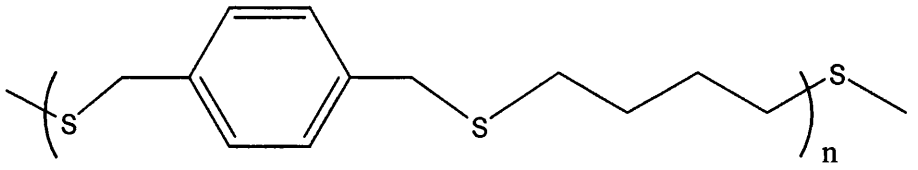
Standard Method A conditions were applied and the following amounts were used- 1,3-propanedithiol (1.50 ml, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), α,α'-dibromo-*p*-xylene (3.56 g ,13.5 mmol) in dry THF (10 mL) and 1-bromobutane (0.41 g, 3.0 mmol). After filtration, washing and drying, a white powder (1.72 g, 55 %) was obtained.



^{1}H-NMR ($CDCl_3$) δ 1.67 (2H, quintet, J = 7 Hz, $CH_2CH_2CH_2$), 2.25 (4H, t, J = 7 Hz, $CH_2CH_2CH_2$), 3.60 (4H, s, $ArCH_2S$) 7.25 (4H, s, ArH). FTIR (neat) *v* 821 (C-H wag, *para*), 770 (probably C-S str), no C-Br str. GPC M_n 4780.

4.5.6 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylenesulfanediylbutane-1,4-diyl.

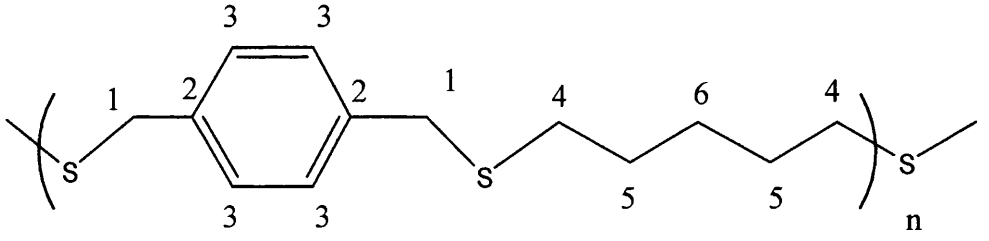
The standard Method A conditions were applied and the following amounts were used: 1,4-butanedithiol (1.75 ml, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), α,α'-dibromo-*p*-xylene (3.56 g ,13.5 mmol) in dry THF (10 mL) and 1-bromobutane (0.41 g, 3.0 mmol). After filtration washing and drying a white powder (1.88 g, 56 %) was obtained.



FTIR (neat) *v* 821 (C-H wag, *para*), 678 (probably C-S), no C-Br str.

4.5.7 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylenesulfandiylpentane-1,5-diyl)

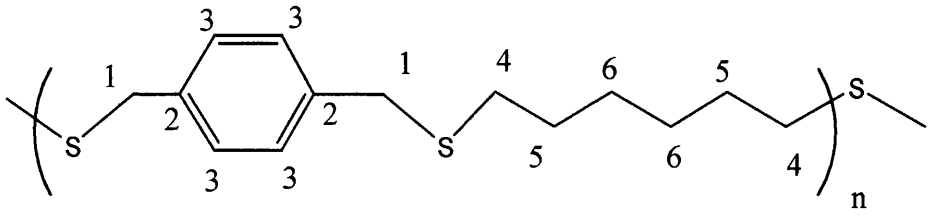
The standard Method A conditions were applied and the following amounts were used- 1,5-pentanedithiol (2.00 ml, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), α, α'-dibromo-*p*-xylene (3.56 g ,13.5 mmol) in dry THF (10 mL) and 1-bromobutane (0.41 g, 3 mmol). After filtration, washing and drying, a white powder (2.46 g, 69 %) was obtained.



^{1}H-NMR ($CDCl_3$) δ 1.00-1.50 (6H, m, $SCH_2CH_2CH_2CH_2CH_2S$) 2.45 (4H, t , J = 7.5 Hz, $SCH_2CH_2CH_2CH_2CH_2S$) 3.60 (4H, s, $ArCH_2S$) 7.25 (4H, s, aromatic).^{13}C-NMR δ 28.1 (C6), 29.2 (C5), 32.3 (C4), 36.4 (C1), 129.4 (C3), 137.6 (C2). FTIR (neat) *v* 819 (C-H wag, *para*), 679 (probably C-S), no C-Br str. GPC M_n 3790.

4.5.8 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylenesulfanediylhexane-1,6-diyl)

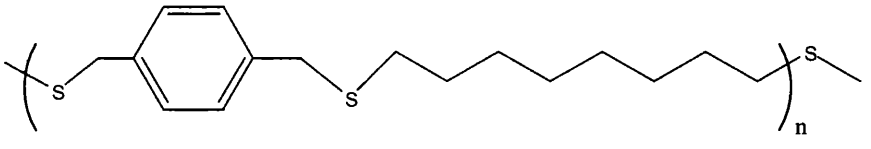
The standard Method A conditions were applied and the following amounts were used- 1,6-hexanedithiol (2.3 ml, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol) α,α'-dibromo-*p*-xylene (3.56 g, 13.5 mmol) in dry THF (10 mL) and 1-bromobutane (0.41 g, 3.0 mmol). After filtration washing and drying a white powder (1.47 g, 65 %) was obtained.



^{1}H-NMR ($CDCl_3$) δ 1.30 (4H, t. J = 7 Hz $SCH_2CH_2CH_2CH_2CH_2CH_2S$), 1.40-1.55 (4H, m, $SCH_2CH_2CH_2CH_2CH_2CH_2S$), 2.40 (4H, t, J = 7.5 Hz, $SCH_2CH_2CH_2CH_2CH_2CH_2S$), 3.40 (4H, s, SCH_2Ar), 7.15 (4H, s, ArH). ^{13}C-NMR δ 28.5 (C6) 28.8 (C5), 31.8 (C4), 36.6 (C1), 129.6 (C3), 137.6 (C2). FTIR (neat) *v* 821 (C-H wag, *para*), 688 (probably C-S) no C-Br str.

4.5.9 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylenesulfanediyloctane-1,8-diyl).

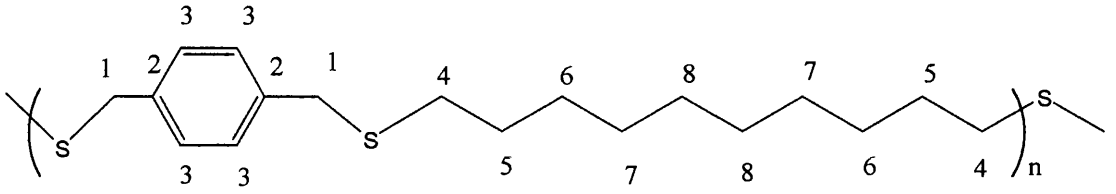
The standard Method A conditions were applied and the following amounts were used: 1,8-octanedithiol (2.75 ml, 15 mmol), dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), α,α'-dibromo-*p*-xylene (3.56 g ,13.5 mmol) in dry THF (10 mL) and 1-bromobutane (0.41 g, 3.0 mmol). After filtration washing and drying a white powder (2.18 g, 52 %) was obtained.



^{1}H-NMR ($CDCl_3$) δ 1.15-1.70 (12H, m, $SCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2S$), 2.35 (4H, t, J = 7.5 Hz , $SCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2S$), 3.60 (4H, s, $ArCH_2S$), 7.30 (4H, s, aromatic). FTIR (neat) *v* 823 (C-H wag, *para*), 679 (probably C-S) no C-Br str.

4.5.10 Synthesis of poly(sulfanediylmethylene-1,4-phenylenemethylenesulfanediyldecane-1,10-diyl)

The standard Method A conditions were applied and the following amounts were used- 1,10-decanedithiol (3.10 g, 15 mmol) in dry THF (20 mL), butyllithium (2.5M, 12 mL, 30 mmol), α,α'-dibromo-*p*-xylene (3.56 g, 13.5 mmol) in dry THF (10 mL) and 1-bromobutane (0.41 g, 3.0 mmol). After filtration washing and drying a white powder (2.40 g, 52 %) was obtained.

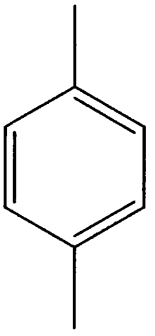


^{1}H-NMR ($CDCl_3$) δ 1.25-1.40 (12H, m, $SCH_2CH_2(CH_2)_6CH_2CH_2S$), 1.55 (4H, m, $SCH_2CH_2(CH_2)_6CH_2CH_2S$), 2.37 (4H, t, J = 7.5 Hz, $SCH_2(CH_2)_8CH_2S$), 3.65 (4H, s, $ArCH_2S$), 7.32 (4H, s, ArH).^{13}C-NMR ($CDCl_3$) δ 29.3, 29.4, 29.6, 29.9 (C5-C8) 32.2 (C4), 36.4 (C1), 129.32 (C3), 137.7 (C2). FTIR (neat) *v* 820 (C-H wag, *para*), 679 (probably C-S). GPC M_n 4710.

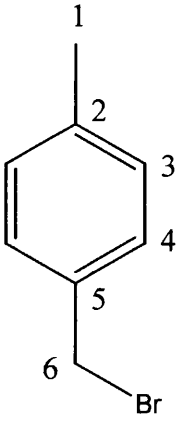
4.5.11 Synthesis of 1,4-bis(bromomethyl)benzene by hydrobromic acid substitution of the equivalent diol.

Hydrobromic acid (7.15 mL, 42.3 mmol, 48 %) was added to a 50 mL round bottomed flask. Concentrated sulfuric acid (4.55 mL, 85.0 mmol) was added slowly over a duration of approximately 45 minutes. 1,4-Cyclohexanedimethanol (3.06 g, 21.3 mmol) was then added to the flask. The mixture was allowed to stir for 24 h. The mixture was then refluxed for 3 h. The reaction was allowed to cool and was then quenched with water (50 mL) and extracted into dichloromethane (50 mL x 2). The organic phases were removed and combined and were then washed with saturated Na_2CO_3 solution (2 x 50 mL). The organic phase was then dried over $MgSO_4$ for 30 minutes. The drying agent was filtered off and the solvent was removed by rotary evaporation. The crude product (4.67 g) was initially distilled at 15mmHg of pressure in order to isolate any *p*-xylene formed. *p*-Xylene (0.213 g, 9.5 %) was obtained at

50°C. Lit.[8] 138°C at ambient pressure. The remaining material was separated by column chromatography using silica as the stationary phase and hexane as the eluent, two main components were isolated. The first component (1.29 g, 33 %) of 1-(bromomethyl)-4-methylbenzene was isolated; the second component (2.88 g, 50 %) was isolated and confirmed as the desired product with trace amounts of impurities present.



^{1}H-NMR ($CDCl_3$) δ 2.40 (6H, s, CH_3), 7.15 (4H, s, ArH). ^{13}C-NMR ($CDCl_3$) δ 21.4 (CH_3), 129.4 (C-H, Ar) 135.1 (C, Ar). FTIR (neat) *v* 793 (C-H wag, *para*). MS EI^+ m/z 106 ($[M]^+$, 35 %), 91.0 ($[M\text{-}CH_3]^+$, 100 %). HRMS EI^+ m/z calcd for $[M]^+$106.0776, found 106.0776.



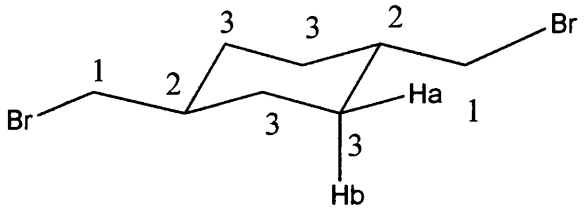
^{1}H-NMR ($CDCl_3$) δ 2.25 (3H, s, CH_3), 4.40 (2H, s, CH_2Br), 7.10, 7.20 (4H, d, J = 8 Hz, d, J = 8.5 Hz, C3H, C4H).^{13}C-NMR ($CDCl_3$) δ 21.4 (C1), 34.2 (C6), 129.6, 129.8 (C3/C4), 135.3 (C5), 138.8 (C2). MS EI^+ m/z 187 ($[^{81}BrM+H]^+$, 50 %),185 ($[^{79}$ Br $M+H]^+$, 40 %), 107 ($[M\text{-}Br]^+$, 100 %), 91 ($[M\text{-}CH_2Br]^+$, 55 %), 81 (30 %), 79 (30 %), 53 (45 %).

4.5.12 Synthesis of *cis*- and *trans*-1,4-bis(bromomethyl)cyclohexane, by PBr_3 substitution of the corresponding diols.

A mixture of *cis*- and *trans*-4-(hydroxymethyl)cyclohexylmethanol (5.0 g, 35 mmol) was dissolved in dry toluene (20 mL) in an oven dried 100 mL round bottom flask. The atmosphere was kept inert by a nitrogen gas flow. Phosphorus tribromide (9.40 g, 35 mmol) was dissolved in dry toluene (40 mL) in a separate dry 50 mL round bottomed flask. The phosphorus tribromide solution was added slowly to the diol solution over 1 hour *via* a dry syringe. The reaction was allowed to stir for 6 h. A reflux condenser was then added and the vessel was heated until reflux. The reflux was allowed to proceed overnight. Overnight the solution had turned from colourless to deep orange. The crude reaction mixture was left to cool for about 2 h and was then poured very slowly into ice water (40 mL), where upon effervescence occurred. The resulting mixture was then stirred vigorously for 2 h. The toluene layer was separated and the water layer was re-extracted with DCM (2 x 40 mL). The organic phases were combined and more DCM (about 100 mL) was added to ensure that there was a sufficient amount of heavy DCM to overpower the light toluene and therefore form only two layers with the organic layer at the bottom in the washing steps. The organic phase was washed with saturated aqueous Na_2CO_3 (2 x 40 mL) and brine (2 x 40 mL). The organic phases were dried over $MgSO_4$ for 45 minutes. The drying agent was filtered off and the DCM and toluene were removed by rotary evaporation. The crude product was subjected to column chromatography to give a colourless oil (5.21 g). The column product was allowed to stand overnight by which time white crystals had formed and were present in a small pool of a liquid. The white crystals were isolated from the liquid product by suction filtration. The liquid product was flushed through with water as any non polar organic solvent would also dissolve the crystalline material. The crystals were then dissolved in a minimum amount of hot toluene and were then allowed to re-crystallise in a refrigerator overnight. After filtration and drying under a vacuum pump the final white crystals (3.20 g, 33.8 %) were obtained and confirmed as the *trans*- product. Mp 54-55 °C. Lit.[9] 55 °C . The aqueous filtrate, which contains water and the liquid material that was originally present alongside the crystalline material prior to filtration was then extracted with hexane (2x 100 mL). The hexane was dried over $MgSO_4$ overnight. The drying agent was filtered off and then the hexane was removed by rotary evaporation. The resulting

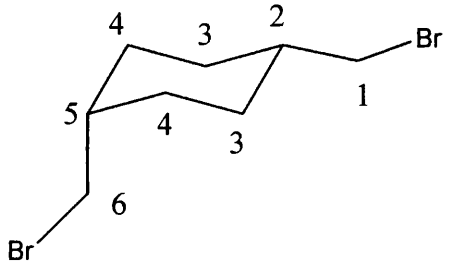
crude product was subjected to reduced pressure fractional distillation (2mmHg) using a vigreux column. One component confirmed as the *cis-* isomer was isolated (1.12 g, 12 %) at 170 °C. Lit.[10] 121 °C at 0.1 mmHg.

trans Product-



^{1}H-NMR ($CDCl_3$)δ 1.10 (4H, m, Hb), 1.63 (2H, m, C2H), 1.97 (4H, m, Ha), 3.35 (4H, d, J = 6.5 Hz, CH_2Br). ^{13}C-NMR ($CDCl_3$) δ 31.4 (C3), 40.2 (C2), 40.4 (C1). FTIR (neat) *v* 647 (C-Br str). MS EI$^+$ m/z 191 ([(M 2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{79}Br,^{81}Br)-^{79}Br]$^+$, 20 %) 189 ([M(2 x ^{79}Br)- ^{79}Br]$^+$/ [M(^{79}Br, ^{81}Br)-^{81}Br]$^+$, 20 %), 109 (C_8H_{13}, 100%) 95 (C_7H_{11}, 90 %) 67 (C_5H_7, 70 %) 55 (50 %). HRMS EI$^+$ m/z calcd for [M(2 x ^{79}Br)]$^+$ 267.9457, found 267.9458.

cis- Product-



^{1}H-NMR ($CDCl_3$) δ 1.10-2.20 (10H, multiple signals, ring protons), 3.35, 3.45 (4H, d, J = 7, d, J = 6.5 Hz, C6H_2Br, C1H_2Br). ^{13}C-NMR ($CDCl_3$) δ 27.4 (C3), 31.4 (C4), 38.0 (C2), 38.6 (C5), 40.2 (C1), 40.4 (C6). FTIR (neat) *v* 680 (C-Br str). MS EI$^+$ m/z 191 ([(M 2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{79}Br,^{81}Br)-^{79}Br]$^+$, 5 %), 189 ([M(2 x ^{79}Br)- ^{79}Br]$^+$/ [M(^{79}Br, ^{81}Br)-^{81}Br]$^+$, 5 %), 109 (C_8H_{13}, 100 %), 95 (C_7H_{11}, 90 %), 67 (C_5H_7, 75 %). HRMS EI$^+$ m/z calcd for [M(2 x ^{79}Br)]$^+$ 267.9457, found 267.9456).

4.5.13 Synthesis of poly(sulfanediylmethylenecyclohexane-1,4-diylmethylene).

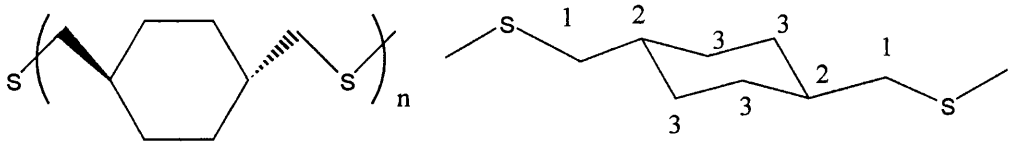
The mixture of *cis-* and *trans*-1,4-bis(bromomethyl)cyclohexane (2.00 g, 7.4 mmol) was heated to 170°C in a 25 mL round bottomed flask in the presence of $Na_2S.9H_2O$ (2.66 g, 11.1 mmol) for 6 hours. Water (10 mL) and DCM (10 mL) were then added. The organic phase was separated and the aqueous phase was extracted twice more with DCM (2 x 15 mL). The organic phases were combined and dried over $MgSO_4$ for 1 hour. The drying agent was then filtered off. The solvent was removed by rotary evaporation to give the crude product (0.832 g). The ^{1}HNMR spectrum revealed the reaction had not proceeded to a significant extent as 66% of the original CH_2Br groups remained and only 34 % of the desired CH_2S groups had formed.

The reaction was repeated using the trans only dibromide and allowed to proceed for 24 hours. After work up a thick colourless crude oil (0.432 g, 41 %) was isolated. ^{1}HNMR analysis was used to determine that only 6% of the original CH_2Br remained.

The reaction was also conducted using the refluxing ethanol method. This reflux in ethanol method was also applied to the cis- only product. For the *trans* only dibromide the thick crude oil obtained (0.461, 43 %) was shown to have only 4 % of the remaining CH_2Br and therefore 96 % of the desired CH_2S groups.

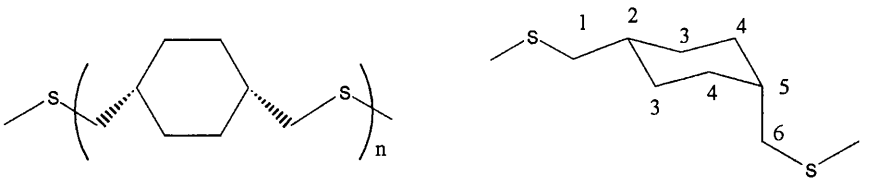
When the *cis-* only dibromide was used the crude oil product obtained (0.521, 49 %) was shown to have only 2 % CH_2Br groups remaining.

trans-



^{1}H-NMR ($CDCl_3$) δ 0.90-2.00 (10H multiple signals, cyclohexane ring protons), 2.40 (4H, d, J = 7 Hz, CH_2S). ^{13}C-NMR ($CDCl_3$) δ 32.8 (C3), 38.5 (C2), 40.9 (C1). FTIR (neat) *v* 756 (probably C-S str), no C-Br str. GPC M_n 814.

cis-

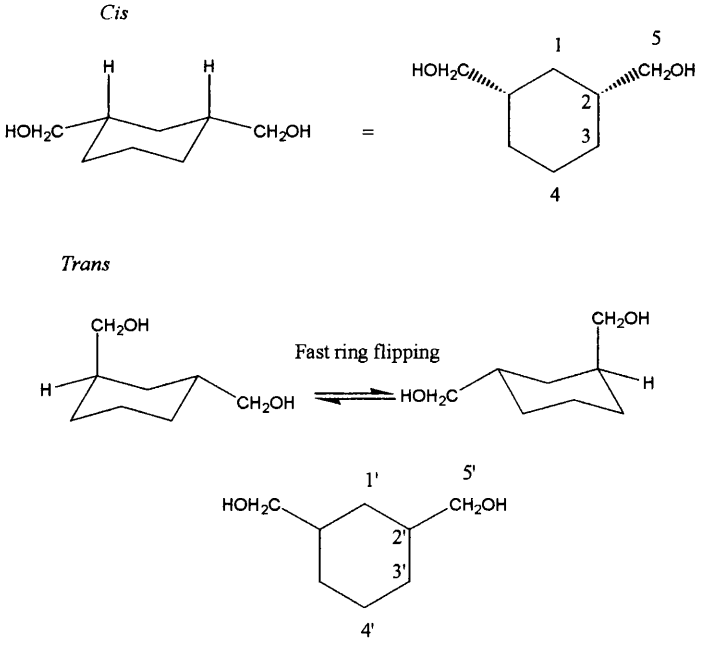


^{1}HNMR ($CDCl_3$) δ 0.90-2.00 (10H multiple signals, aliphatic ring protons), 2.55, 2.65 (4H, d, J = 7 Hz, d, J = 6.5 Hz, $C1H_2S$, $C6H_2S$). ^{13}C-NMR ($CDCl_3$) δ 28.5 (C3), 32.9 (C4), 37.8 (C2), 38.0 (C5), 40.6, 40.4 (C1, C6). FTIR (neat) *v* 755 (possibly C-S), no C-Br str. GPC M_n 705.

4.5.14 Synthesis of 3-(hydroxymethyl)cyclohexylmethanol

The standard diborane reduction described in Section 3.10.4 was followed and the following amounts were used: BF_3Et_2O (1.2 mL, 7.6 mmol) in dry THF (40 mL), mixture of *cis-* and *trans*-cyclohexane-1,3-dicarboxylic acid (1.0 g, 5.1 mmol) and $NaBH_4$ (0.66 g, 17.4 mmol) in dry THF (40 mL). The crude product was subjected to kuglerohr distillation at 2mmHg of pressure. One component was isolated (0.81 g, 97 %) at 100-125° C. Lit.[11] 112° C at 1mmHg.

The procedure followed was scaled up; cyclohexane-1,3-dicarboxylic acid (5.0 g, 25.5 mmol) was used. After work-up the diol (4.09 g, 98 %) was isolated by reduced pressure distillation.



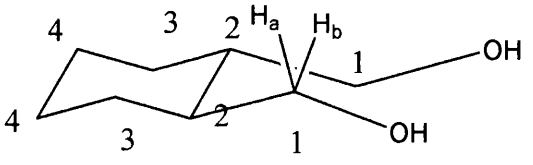
Observed time averaged species by ^{13}CNMR

^{1}H-NMR ($CDCl_3$) δ 0.7- 1.0 (2H, m, C2*H* C2'*H*), 1.4-2.0 (8H, protons on C1/C1', C3/C3', C4/C4'), 3.35-3.52 (4H, m, CH_2OH), 3.30 (2H, OH, D_2O exchangeable).^{13}C-NMR ($CDCl_3$) δ 21.4, 25.7 (C4 and C4'), 28.8, 29.8 (C3 and C3') 30.3, 33.1 (C1 and C1'), 35.3, 40.4 (C2 and C2') 66.4, 68.8 (C5 and C5'). FTIR (neat) *v* 3300 (OH *str*). MS $CI^+(NH_3)$ m/z 162 ($[M+NH_4]^+$, 100 %). EI^+ m/z 95 (C_7H_{11}, 100 %), 67 (C_5H_7, 80 %).

4.5.15 Synthesis of *trans*-2-(hydroxymethyl)cyclohexylmethanol

The standard diborane reduction described in Section 3.10.4 was followed and the following amounts were used: BF_3Et_2O (1.2 ml, 7.55 mmol) in dry THF (40 mL), *trans*-cyclohexane-1,2-dicarboxylic acid (1.0 g, 5.1 mmol) and $NaBH_4$ (0.66 g, 17.4 mmol) in dry THF (40 mL). The crude product was subjected to kuglerohr distillation at 4mmHg of pressure. One component was isolated (0.82 g, 98 %) at 140-150 °C. Lit[12]. 125°C at 3mmHg. The product was then allowed to cool and solidify and was then re-crystallised from hot methanol. GC of the product indicated that there was only one component present which was expected due to the use of the *trans* only starting material.

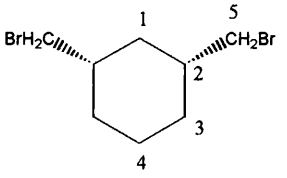
The procedure followed was scaled up and after work-up the diol (2.94 g, 97 %) was isolated by reduced pressure distillation.



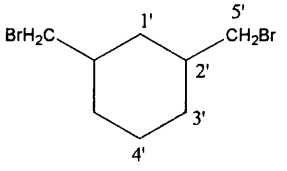
^{1}H-NMR ($CDCl_3$) δ 0.95 (2H, m, C2*H*), 1.10-1.65 (8H, CH_2 ring protons), 3.20 (2H, D_2O exchangeable, OH), 3.40 (2H, dd, J = 11, 7 Hz, CH_aBr) 3.53 (2H, dd, J = 11, 3 Hz, CH_bBr).^{13}C-NMR ($CDCl_3$) δ 26.5 (C4), 30.2 (C3), 45.1 (C2), 68.2 (C1). FTIR (neat) *v* 3307 (OH *str*). MS m/z CI^+ (NH_3) 162 ($[M+NH_3]^+$,65 %), 158 (100 %), 145 ($[M-OH+NH_4]^+$, 30 %). EI^+ m/z 95 (C_7H_{11}, 30%) 67 (C_5H_7, 90 %) 41 (100 %).

4.5.16 Synthesis of 1,3-bis(bromomethyl)cyclohexane

The phosphorus tribromide substitution method as described in Section 4.5.12 was followed and the following amounts were used: mixture of *cis*- and *trans*-3-(hydroxymethyl)cyclohexylmethanol (2.33 g, 16 mmol), phosphorus tribromide (1.52 mL, 16 mmol) and toluene (20 mL). The crude product was partially purified by column chromatography as determined by TLC analysis. The main column fraction was then subjected to reduced pressure distillation (5mmHg, 115 °C) to give a colourless oil (2.11 g, 48 %). Lit.[11] 93 °C at 0.4 mmHg.



Cis



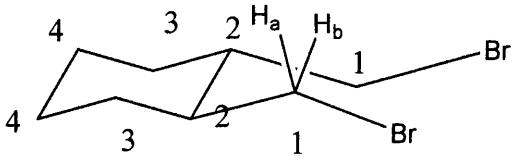
Time averaged trans

^{1}H-NMR ($CDCl_3$) δ 0.75-1.00 (2H, m, C2*H*, C2'*H*), 1.20-2.05 (8H, protons on C1/C1', C2/C2'-C4/C4'), 3.20-3.45 (4H, m, CH_2Br).^{13}C-NMR ($CDCl_3$) δ 20.6, 25.6 (C4 and C4'), 30.42, 31.63 (C3 and C3'), 34.52, 37.00 (C1 and C1'), 35.57, 38.79 (C2 and C2') 40.03, 40.51 (C5 and C5'). FTIR (neat) *v* 642 (C-Br str).
MS

4.5.17 Synthesis of *trans*-1,2-bis(bromomethyl)cyclohexane

The phosphorus tribromide substitution method as described in Section 4.5.12 was followed and the following amounts were used: *trans*-2-(hydroxymethyl)cyclohexylmethanol (2.00 g, 13.9 mmol), phosphorus tribromide (1.30 mL, 13.9 mmol) and toluene (25 mL). Analogously to the previous reaction, the crude product was partially purified by column chromatography as

determined by TLC analysis. The main column fraction was then subjected to reduced pressure distillation to give colourless clear oil (2.02 g, 54 %).



^{1}H-NMR ($CDCl_3$) δ 1.17 (2H, C2*H*), 1.25-1.80 (8H, CH_2 ring protons), 3.40 (2H, dd, J = 10.5 Hz and 1.5 Hz, CH_aBr) 3.50 (2H, dd, J = 10.5, 4 Hz, CH_bBr). ^{13}C-NMR ($CDCl_3$) δ 26.0 (C4), 31.0 (C3), 39.5 (C1), 40.4 (C2). FTIR (neat) *v* 653 (C-Br str). MS m/z EI$^+$ 191 ([(M 2 x ^{81}Br)-^{81}Br]$^+$/ [M(^{79}Br,^{81}Br)-^{79}Br]$^+$, 5 %) 189 ([M(2 x ^{79}Br)-^{79}Br]$^+$/ [M(^{79}Br, ^{81}Br)-^{81}Br]$^+$,5 %), 109 (C_8H_{13}, 100 %), 95 (C_7H_{11}, 90 %), 67 (C_5H_7, 60 %), 41 (40 %).

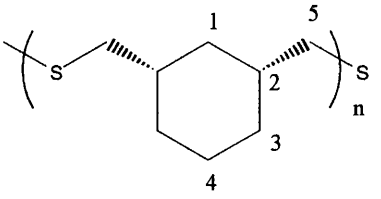
4.5.18 Synthesis of poly(sulfanediylmethylenecyclohexane-1,3-diylmethylene) (Polymer 13).

A mixture of *cis*- and *trans*-1,3-bis(bromomethyl)cyclohexane (1.00 g, 3.7 mmol) was heated to 170°C in a 25 mL round bottomed flask in the presences of $Na_2S.9H_2O$ (1.22 g 5.5 mmol) for 24 hours. Water (10 mL) and DCM (10 mL) were then added. The organic phase was separated and the aqueous phase was extracted twice more with DCM (2 x 15 mL). The organic phases were combined and dried over $MgSO_4$ for 1 hour. The drying agent was filtered off. The solvent was then removed by rotary evaporation to give a crude colourless oil (0.215 g, 41 %) . ^{1}HNMR revealed that the reaction had proceeded, but not to the desired extent. The proton integration showed that 32 % of the original CH_2Br groups remained relative to the newly formed CH_2S groups.

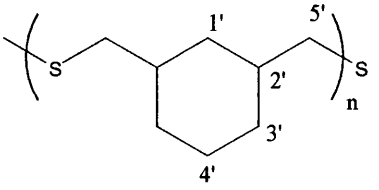
The reaction was repeated and allowed to proceed for 48 hours. After work up a crude clear thick oil (0.164 g, 37 %) was isolated. This time the proton integration showed that 27 % CH_2Br groups remained and only 73 % of the desired CH_2S group had formed.

The reaction was also carried out under refluxing ethanol conditions. After work-up the crude clear oil was obtained (0.332 g, 63 %). The ^{1}HNMR spectrum

indicated that < 3 % CH_2Br group remained and therefore the desired CH_2S groups were present in a significant abundance.



Cis



Time averaged *Trans*

^{1}H-NMR ($CDCl_3$) δ 0.90-2.00 (10H, m, aliphatic ring protons), 3.20-3.50 (4H, m, CH_2S). ^{13}C-NMR ($CDCl_3$) δ 20.8, 25.6 (C4, C4'), 30.20, 32.00 (C3, C3'), 35.00, 37.00 (C1, C1'), 35.6, 39.8 (C2, C2'), 38.5, 40.4 (C5, C5').

GPC M_n 1550.

4.5.19 Attempted Synthesis of poly(sulfanediylmethylenecyclohexane-1,2-diylmethylene)

trans-1,2-Bis(bromomethyl)cyclohexane (0.75 g, 2.80 mmol) and $Na_2S.9H_2O$ (1.0 g, 4.17 mmol) were placed in a 5 mL round bottom flask fitted with a reflux condenser. The flask was heated to 170°C and left for 24 hours. The reaction mixture was transferred to a beaker and was quenched with water (10 mL) and DCM (10 mL). The organic phase was separated and the aqueous phase was extracted twice more with DCM (2 x 10 mL). The organic phases were combined and dried over $MgSO_4$ for 1 hour. The drying agent was filtered off. The solvent was removed by rotary evaporation to give a crude oil (0.065 g).

The reaction was repeated and allowed to proceed for 24 hours. A crude oil colourless oil was obtained (0.036 g).

The reaction was also carried out using the refluxing ethanol method. A crude oil was obtained (0.040 g).

The proton NMR of all the crude products obtained from these reactions indicated that the desired CH_2S groups had formed, but there was also significant amounts of aromatic material and remaining CH_2Br groups, as well as other unassigned signals.

4.6 Final Conclusion

Numerous linear polythiaalkanes have previously been synthesised at the Centre of Clean Chemsitry.[2] This thesis reports the successful synthesis of numerous novel thiapolymers including polymers with branched (methyl) groups, aromatic ring units and aliphatic rings units. A series of tetrahydrothiopyrans with various degrees of methyl substitution was also synthesised.

The novel polymeric materials and cyclic sulfides synthesised were all tested as potential selective catalysts for the chlorination of phenol, *o*-cresol, *m*-cresol and *m*-xylenol. Where feasible comparison to their polymeric linear analogues was also made.

As a result of this extensive investigation numerous novel sulfide based catalysts have shown to give excellent levels of regioselectivity for the chlorination of phenols with sulfuryl chloride in the presence of Lewis acid co-catalysts.

Polymer 2 (poly[sulfanediyl(1,6-dimethylhexane-1,6-diyl)]) synthesised as reported in chapter 2 was shown to behave as a highly selective catalyst for the chlorination of *m*-xylenol. A *para*:*ortho* selectivity ratio in excess of 40 and a yield of approximately 95 % of **PCMX** was obtained in the presence of only 10 mg of **Polymer 2** and 25 mg of Lewis acid when 50 mmol of *m*-xylenol was reacted with 55 mmol of sulfuryl chloride.

The tetrahydrothiopyrans synthesised as reported in chapter 3 were shown to behave as excellent catalysts for the chlorination of *o*-cresol with *para*:*ortho* selectivities in excess of 40 and yields of **PCOC** as high as 96.6% were obtained.

Out of the ring containing thiapolymers synthesised as reported in chapter 4, **Polymer 13** [poly(sulfanediylmethylenecyclohexane-1,3-diylmethylene)] was shown to be the most generically selective catalyst for the chlorination of phenols, with yields as high as 95.4, 93.6 and 93.8 % of **PCOC**, **PCMC** and **PCMX** obtained respectively.

The increased regioselectivity observed when these novel polymeric materials were used as catalysts was probably the result of increased steric bulk in the vicinity of the catalytic sulfur atoms. Future studies may be best conducted by investigating the specific interactions that take place between the catalytic sites and the phenolic compounds. This may be achieved by the use of computer modelling followed by the synthesis of molecules which are predicted to interact with the phenolic compounds in such a way that substitution occurs regioselectively.

4.7 References

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